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, the region’s only academic health system.

discoveries.ucsd.edu
Even as we parse ever more finely the natures of cells and molecules, science allows us to also pull back to uncover previously unseen biological systems and networks, revealing the secrets of human health writ small and large.
“From the molecular machinery of mitochondria to laden winds blowing over oceans and ourselves; from the Petri dish to the person...these lessons can make us smarter, happier and healthier.”

David A. Brenner, MD
THE HUMAN BODY IS A MASTERPIECE
OF MASTERED PIECES

Molecules making cells; cells coordinating
to create networks; networks forming tissues
and organs; organs combining to, well,
comprise each of us.

Peer deep within our many and different
biologies or pull back to see the bigger
picture, and new marvels are invariably
revealed. It’s a fact that I am reminded of
daily by the work and achievements of my
colleagues – the scientists, physicians and
staff at UC San Diego.

This year’s issue of Discoveries celebrates
that marvelous reality of duality. It is the
idea that we can learn at every level of
our biological existence: from the molecular
machinery of mitochondria to laden winds
blowing over oceans and ourselves; from
the Petri dish to the person, and that these
lessons can make us smarter, happier
and healthier.

That has been the history at UC San Diego
Health Sciences and UC San Diego Health.
We are leaders in Alzheimer’s disease, cancer
and stem cell research. We have advanced
those fields measurably and will continue to
do so. Our physicians have pioneered surgical
techniques, devices and technologies that
save lives. Our scientists across departments
and disciplines have and continue to describe
new and fundamental facets of life, how they
function and fit together, in ways big and small.

Their work, of course, could not progress as
quickly or as far without the extraordinary
support of donors, such as Joan and Irwin
Jacobs, Denny Sanford, Pauline Foster,
Evelyn and Ernest Rady, Carol Vassiliadis and
others whose philanthropic generosity helps
drive our enterprise, from the lab to the clinic.

You can read about some of these efforts
in the magazine you’re holding – from
the surprising science of the emergency
room and the human gut to the growing
importance of training new generations of
pharmacists and identifying the needs of
older generations of Americans.

These articles do not tell the whole story,
of course, no more than the rising, shining
edifices of Jacobs Medical Center and the
Altman Clinical and Translational Research
Institute (both slated to open in 2016) reveal
the wonders and work that will happen within.

They are but peeks at the present and hints
of the future, one that is bright with the
promise of ourselves. Here’s to looking at
you, us and ahead.

Sincerely,
David A. Brenner, MD
Vice Chancellor, Health Sciences
and Dean, School of Medicine
University of California, San Diego

Photograph by Alin Cibian
We are defined by our memories, but what defines a memory, particularly at the cellular level?

Photograph by David Ahnholz
“We are really starting to understand the molecular basis of memory formation and how to modify it.”

Roberto Malinow, MD, PhD

"IT’S ALL ABOUT THE SYNAPSE," said Roberto Malinow, MD, PhD, professor of neurosciences and Shiley Endowed Chair in Alzheimer’s Disease Research in Honor of Dr. Leon Thal. It's all about what happens in the tiny gap between neurons across which signals pass.

Malinow should know. He and colleagues have shown that by manipulating the strength of synaptic communications in the brains of rats, they can implant, erase and predictably reactivate a specific memory.

“We can play with memory like it’s a yo-yo, by strengthening or weakening the appropriate synapses.”

The research provides some of the most direct evidence yet that memory formation is biologically rooted in the selective strengthening of neuronal connections. Weaken these connections and the memory is lost; re-strengthen them and the memory is restored.

The idea is not new, said Malinow, “but our research offers the strongest case so far that the plasticity of the brain resides in the complex functioning of the synapse.”

SEEING IS BELIEVING

Malinow’s team re-enacted classical Pavlovian experiments with rats but employed a new technology – optogenetics – to activate neurons using pulses of light delivered through a thin fiber optic cable. Neurons were made sensitive to light with a virus modified to carry a gene that codes for a light-sensitive protein.

Scientists taught the rats to associate optogenetic stimulation of auditory neurons (similar to hearing a tone) with fear by applying a mild foot shock every time the rats’ auditory neurons were stimulated.

Brain tissue analyses showed that a cellular change known as long-term potentiation (LTP) occurred in the synapses of affected rats. A synapse that has undergone LTP is believed to be more likely to transmit a signal to adjoining neurons. Long-term depression (LTD) has the opposite effect. Receptors are removed, resulting in a weaker synapse.

Sadegh Nabavi, PhD, a member of Malinow’s lab, then stimulated the same neurons with a low-frequency train of light pulses, which is widely known to cause LTD. The rats no longer froze at the optogenetic neuron stimulation, suggesting the fearful memory had been erased or at least inactivated.

Intriguingly, the rats’ conditioned fear response could be resurrected by re-strengthening the synapses by stimulating the same auditory neurons with a memory-forming, high-frequency train of light pulses. “The fascination is observing how profoundly we can modify behavior by manipulating a relatively few number of neurons,” Malinow said. “We are really starting to understand the molecular basis of memory formation and how to modify it.”

Although the experiments are not appropriate for human testing, Malinow receives frequent requests from people asking if he can help them erase painful memories. Developing such a therapy is plausible. UC San Diego researchers are currently using rats to test a drug designed to lower the threshold for LTD.

“Our hope is that we can inactivate the animals’ associative memory of the foot shock, similar to what we did with the low-frequency pulses of light, but with a combination of behavioral training and drugs,” said Malinow.

Ultimately, the idea would be to administer a drug and then ask the patient to recall the bad memory. The drug would selectively activate in synapses representing that memory, weakening them and thus diminishing the memory's intensity.

“People’s traumatic memories are complex,” said Malinow, “but the general principle that it’s possible to inactivate a bad memory is scientifically valid.”

Memory manipulation research has potential applications for hard-to-treat disorders such as dementia and PTSD. Help accelerate development of new treatments by making a gift online at giving.ucsd.edu or calling 858-822-4562.
Trauma as a Preventable Disease

In the whirl of the trauma center, scientists seek ways to help people avoid it.

LIFE IN THE TRAUMA CENTER AT UC SAN DIEGO MEDICAL CENTER IN HILLCREST IS OFTEN FRAUGHT. As the region’s first Level 1 trauma center, it is often the go-to place for patients with symptoms or injuries that may transcend the capabilities and resources of ordinary hospital emergency rooms.

Here, doctors, nurses and staff tend to more than 3,200 patients each year, including victims of motor vehicle collisions, falls, violence, near drowning and fire, often with injuries grievous and life-threatening.

The visible world and whirl of trauma care is frequently rushed and noisy, infused with the seemingly chaotic imperative of life and death. But behind it lies something else: science. Trauma research may seem a contradiction in terms, but it drives the overall goal of improving the outcomes of patients who find themselves unexpectedly, terrifyingly, in need of emergency health care.

“It goes even further,” said Raul Coimbra, MD, PhD, FACS, surgeon-in-chief at medical center and chief of the division of trauma, surgical critical care, burns and acute care surgery in the School of Medicine. “Trauma is a preventable disease. We seek not just excellence in patient care, but the advancement of knowledge and practices that will help prevent trauma in the first place.”

AFTER INJURY, A GENETIC STORM

When people talk about trauma research, said Todd Costantini, MD, assistant professor of surgery and one of eight trauma surgeons at Hillcrest, they are fundamentally asking this question: Why do two people with similar injuries have different outcomes: one quickly recovers while the other does not?

It’s a remarkably difficult question. For physician-scientists like Coimbra, Costantini and their colleagues, at least some answers lie in the immune response: how the body recognizes, reacts to and repairs damage to itself, whether from pathogen or misfortune.

“Immediately after injury, there is a storm of gene activity,” said Costantini. Much of the activity is necessary, beneficial and vital to recovery, he said. But sometimes the response can go awry, leading to catastrophic effects like systemic inflammation, organ failure and death. If researchers can more precisely understand how the immune response works – and doctors can more effectively control it – more trauma patients will presumably recover more quickly and with fewer adverse effects.
1 in 5
U.S. adults reported at least one emergency room visit in the past year

SOURCE: National Hospital Ambulatory Medical Care Survey: 2011
“Not only must we be in a state of readiness 24/7, 365 days a year, but we have to have all of the specialties, all of the resources at hand as well.”

Raul Coimbra, MD, PhD, FACS, Surgeon-in-chief at UC San Diego Medical Center

VAGUS NERVE CONNECTION

“One idea is to ramp up treatment in the ambulance, while the patient is still on the way to the hospital, to prevent some of the earliest immune derangements,” said Costantini. “This is the holy grail: to know what has happened and what has changed in the patient’s body and how the body is responding; to target those changes in beneficial ways; and to do it quickly. The most effective measures, we’ve found, generally happen within a few hours of injury.”

Of particular interest to UC San Diego trauma researchers is the vagus nerve, which weaves from the brain stem to the intestines and abdominal organs, connecting multiple organ systems and modulating a variety of critical body functions, including heartbeat and the muscle movement necessary to breathe.

Andrew Baird, PhD, adjunct professor and vice chair of research in the Department of Surgery, and colleagues have reported that stimulating the vagus nerve via enteric glia – a type of nervous system cell that governs gut function – prevents intestinal inflammation, which can lead to systemic problems and worse. “By activating and harnessing the anti-inflammatory effects of enteric glia cells, we hope to develop therapeutics that improve patient outcomes,” said Baird.

UC San Diego researchers are also probing white blood cells for orphan genes (those with no known function) that may encode hormones involved in the body’s immune response. One such candidate is a gene called ecrg4, which encodes a protein released upon injury. The researchers believe ecrg4, used as a biomarker, might quickly alert physicians about a patient’s state and the extent of the injury, informing their treatment decisions.

TREATING TRAUMA WITH EDUCATION

“People think of trauma as a random, bad event, something that happens and for which there’s not much they can do,” said Costantini. “That’s not entirely true. A lot of trauma is preventable through research and education.”

One such effort is the Training, Research and Education for Driving Safety (TREDS) program, directed by Linda Hill, MD, PhD, professor of family and public health in the School of Medicine. Since 2005, Hill and colleagues have been gathering data about issues that put California motorists at risk of injury and death, from blood alcohol content to distracted driving to impairments of age. Much of this data is used in training programs for doctors and law enforcement to help them recognize drivers who pose a danger behind the wheel.

After a serious injury, doctors typically confront one or more of these life-threatening conditions:

- Shock, typically caused by significant blood loss
- Systemic Inflammatory Response Syndrome
- Acute lung injury
- Acute kidney injury
- Infection/sepsis
- Multiple organ failure

Rush to the emergency room:
The Centers for Disease Control and Prevention estimate Americans visit the ER more than 136 million times each year.

Number of visits related to injury:

40.2 mil

UC SAN DIEGO HEALTH SCIENCES
“People think of trauma as a random, bad event, something that happens and for which there’s not much they can do. That’s not entirely true. A lot of trauma is preventable through research and education.”

Todd Costantini, MD
Assistant professor of surgery

Percent of visits with patient seen in fewer than 15 minutes: 27%
Percent of visits resulting in hospital admission: 11.9%

ROAD TO IMPROVEMENT

“Medically impaired drivers are disproportionately represented in driving crashes, often due to factors associated with aging, such as reduced vision, frailty, cognitive impairment, medication side effects and interactions, and other conditions like Parkinson’s disease, depression and stroke,” said Hill.

“The over-65 population is the fastest-growing demographic in the U.S. By 2030, one in five drivers will be over 65 years of age. While many older adults self-regulate – they stop driving when they are no longer able to do so safely – a significant number do not. The result is a crash rate per distance driven for men over age 80 that is higher than for teenage boys.”

To counter this trend, TREDS trains doctors and law enforcement officers to look for and recognize signals indicating a medically impaired driver. More than 9,000 health care professionals and 4,000 law enforcement officers have gone through the certification process.

Good science demands a sort of plodding methodology: hypothesis, testing, theory, re-testing. Medicine requires clinical trials, which are obviously problematic in trauma centers where doctors never really know the nature of their next case. “And most patients and their families aren’t usually in the mindset to discuss participating in a trial,” said Costantini.

To get around these realities, trauma researchers broadly collaborate, said Coimbra, creating large networks of physician-scientists who can combine their treatment data on, say, burn victims to see larger patterns and potential solutions.

It’s a hugely demanding endeavor.

“If you sustain a life-threatening injury in San Diego County, your odds of surviving are twice those almost anywhere else in the U.S. To support this lifesaving care, call 858-822-4562 or visit giving.ucsd.edu.
More Than a Gut Feeling

Our health relies a lot upon our intestinal multitude

Photographs by David Ahrtholz
It’s never lonely being you. Along with the roughly 34 to 70 trillion cells that comprise the average human body, you are home to perhaps 10 times as many microbial cells. In numbers alone, you’re technically more nonhuman than human.

BUT THESE MYRIAD MICROORGANISMS AREN’T NECESSARILY FREeloadERS
happily hunkering down for a free meal and ride. A slew of studies in recent years suggest the makeup of our microbiomes – the exact microbial species and their relative numbers found on our skin, in our mouths, everywhere – may be essential to our health.

And nowhere is that more appreciated than in our intestines, where the microbiome is under rigorous scrutiny for its role in appetite regulation, weight gain, food allergies, autoimmunity, susceptibility to diseases such as colon cancer and inflammatory bowel disease (IBD), even mood.

Scientists are also investigating how a microbiome can be altered, for better or for worse, by age, diet, antibiotic use, the people you live with, and other environmental and lifestyle factors.

Rob Knight, PhD, is a pioneer in the study of microbiomes. He’s a former Howard Hughes Medical Institute Early Career Scientist who regularly publishes in top scientific journals. He’s a TED talker. A bacterial “fingerprinting” technique he developed was featured on a TV episode of CSI: Miami.

Knight is also co-founder of the American Gut Project. Just as the Human Genome Project set out to sequence the entire human genome, American Gut’s goal is to sequence the human gut microbial population, not just one but tens of thousands of them, since they vary so much between people. While all humans are more than 99.9 percent genetically identical, the makeup of our microbiomes can differ by as much as 90 percent, even among healthy people or people with the same disease.

“But there are some consistencies across microbiomes, depending on the disorder or condition,” Knight says. “With IBD, for example, we’re finding that most people have the same changes in their microbiomes, relative to healthy people.”

American Gut is a crowdsourced, crowdfunded project, which means anyone can submit samples and learn more about their personal gut microbiomes while simultaneously contributing data that can be mined by researchers. Knight hopes that, among many other things, the project will provide new insights into the microbiome’s role in IBD, a family of diseases that includes Crohn’s disease and affects more than one million Americans.

“These similarities and differences in microbiomes provide an exciting opportunity,” said Knight. “By cataloging them, we’re hoping to be able to subtype patients. So, for example, instead of all Crohn’s disease patients being classified the same, maybe one day we’ll be able to group them into distinct populations of Crohn’s; say type 1 and type 2, within a traditional diagnosis of ileal Crohn’s disease. That would allow for more specific diagnoses and perhaps more personalized treatments.”

Knight moved to UC San Diego from the University of Colorado earlier this year, spurred in part by the opportunity to collaborate with computational biologists and clinicians, such as William Sandborn, MD, chief of the division of gastroenterology and director of the Inflammatory Bowel Disease Center at UC San Diego Health. Sandborn directs a large clinical research unit investigating IBD, and has developed new diagnostic techniques and medical therapies.
“For IBD, we’re finding that most people have the same changes in their microbiomes, relative to healthy people.”

Rob Knight, PhD (above)

Sandborn also heads UC San Diego Health’s IBD biobank, a repository that collects and stores patient samples, paired with each individual’s clinical information. The biobank is a bit like the American Gut Project, but it’s specific to IBD patients at UC San Diego Health, which allows Sandborn and his team to collect a greater variety of DNA, blood, stool and biopsy samples, as well as other medical information. The biobank now contains samples from 200 IBD patient volunteers who regularly contribute.

A family history of IBD increases an individual’s risk of developing the disease, Sandborn said, but most people with IBD don’t have any family history. That’s where the gut microbiome may come in.

“There’s obviously more than just genetics at work in IBD,” Sandborn said. “We’ve begun to look at what’s happening in the microbiome of the patients whose samples we have stored in the biobank. We’re also initiating experiments to optimize the selection and dosing of various therapies for IBD. We anticipate these studies will ultimately enable physicians to provide more personalized treatment options to IBD patients.”

While Knight brings his microbiome expertise to bear on IBD and Sandborn his clinical capabilities, Larry Smarr, PhD, brings the software pipelines necessary to make sense of the gushing data.

Smarr is a professor of computer science and engineering at UC San Diego and founding director of the California Institute for Telecommunications and Information Technology, which has divisions at both UC San Diego and UC Irvine. Smarr has been interested in what he calls “digitally enabled genomic medicine” for years and is using the resources of the San Diego Supercomputer Center to study the distribution of the hundreds of bacterial species in the human gut microbiome.

He’s also got a more personal interest. Smarr suffers from colonic Crohn’s disease, a type of IBD. For years, Smarr has been collecting data on himself, everything from whole-genome sequencing to routinely sampling the shifting microbial population of his own gut.

Over the years, Smarr has discovered his gut microbiome is significantly different than that of healthy people. In fact, many of the bacterial species that are most abundant in healthy people are relatively rare in Smarr’s gut. From his genome sequence, he also knows that he has one of the gene variations first discovered to increase a person’s risk for IBD.

Clearly, IBD represents the complex interplay of human genetic variation, dysfunction of the immune system, environmental factors and the microbiome. Knight, Sandborn and Smarr will attack on all fronts.

“As both a patient and a scientist,” said Smarr, “I see this work as a tremendous opportunity to really move the needle in the way we understand and treat IBD, by bringing together supercomputing power, well-characterized patient samples, a variety of animal models and microbial expertise.”
IBD can be debilitating and chronic. The disease often interferes with the personal and work lives of young adults, who face a lifetime battling these symptoms.

Approximately 1.4 million Americans have some form of IBD, a family of diseases that includes ulcerative colitis and Crohn's disease. IBD can vary in severity. Symptoms include abdominal pain, diarrhea, intestinal bleeding, fecal urgency and weight loss. Serious complications such as bowel obstruction, colon cancer, malnutrition and abscesses can also occur, sometimes resulting in surgical removal of portions of the intestine.
The days of treating cancer as a single disease are fast disappearing. Today, oncologists collaborate with scientists, surgeons, geneticists, pathologists and others to treat each patient individually, based upon their cancer types (or subtypes) and unique cellular abnormalities.

“INSTEAD OF STUDYING 1,000 PATIENTS WITH BREAST CANCER and determining the drug with the highest percentage of responders, we’re now looking at each individual tumor to determine the drugs that would work for that patient,” said Razelle Kurzrock, MD, director of the Center for Personalized Cancer Therapy at Moores Cancer Center at UC San Diego Health. “Even if that patient is the only person in the world with that portfolio of abnormalities, we want to treat them.”

Progress is happening quickly, said Kurzrock. A couple of years ago, genomic medicine yielded actionable treatment options in 20 percent of cases, now it’s closer to 90 percent.

For some cancer patients, the best treatment might boost their immune systems. For others, it’s a combination of therapies originally approved for different diseases. For some, it’s a watchful wait-and-see approach.

**IMMUNOTHERAPY**

Immunotherapy is a new approach for a variety of cancers.

“Just like every person’s tumor is different, every person’s immune response against the tumor is different,” said Sandip P. Patel, MD, assistant clinical professor and medical oncologist for Phase I clinical trials and cancer immunotherapy at Moores Cancer Center. “Those differences are responsible for the efficacy of immunotherapy in each patient.”

Immunotherapy involves revving up the body’s own defenses against cancer, by stimulating the immune system to work harder or smarter or providing it with needed components, such as man-made proteins.

An increasing number of cancer types have proven amenable to immunotherapy, such as lung, head and neck, bladder, renal cell and Hodgkin’s lymphoma. Patients with metastatic disease, such as melanoma, can go into remission.

Moores Cancer Center is a top-25 cancer center in the country. To learn more, visit cancer.ucsd.edu; to support cancer research, patient care or training, click on “Make a Donation.”
“Just like every person’s tumor is different, every person’s immune response against the tumor is different.”

Sandip P. Patel, MD

Using genomic sequencing of tumors and immune system analyses, oncologists and scientists are trying to determine what makes a person’s body respond to immunotherapy and, if it doesn’t, what can be done to trigger the immune system to respond as it normally would.

When Jacobs Medical Center at UC San Diego Health opens in 2016, Patel expects to use chimeric antigen receptor–modified T-cell therapies. Here, patients’ own white blood cells are reprogrammed to attack their specific cancers. This therapy has already shown promise in blood cancers, such as acute lymphoblastic leukemia, chronic lymphocytic leukemia and lymphomas.

“Many new clinical trials will involve new checkpoints or targeted therapies in combination with immunotherapy,” said Patel. “It amplifies patients’ own innate immune response to train their immune systems to fight their tumors—not just while they’re being treated, but afterwards. The goal is for patients’ immune systems to take over surveillance.”

**BREAST CANCER**

Personalized medicine using biologic therapies that target only cancer cells has reduced unnecessary or severe treatments for women with breast cancer, said Anne Wallace, MD, director of the Comprehensive Breast Health Center at Moores Cancer Center.

“Ten years ago, if you were 50 years old and had a two-centimeter tumor, you were encouraged to consider chemotherapy,” said Wallace. “In 2015, that’s no longer necessarily true. We evaluate the genetic profile of a patient’s tumor and determine if she really needs chemotherapy or, for example, she might need an anti-estrogen therapy. Personalized medicine is allowing us to do something different for every woman.”

Since joining the I-Spy 2 clinical trial in 2010, the Moores Cancer Center breast cancer team has enrolled more than 100 women. This clinical trial is testing Phase II investigational agents in combination with standard chemotherapy in a curable patient population. The adaptive trial design allows treatment to be tailored to a patient’s specific tumor type, informing treatment options based upon the results of previous trial participants.

“Personalized medicine builds upon multiple components that include genomics, clinical trials, immunotherapy and understanding hereditary abnormalities that may influence a person’s predisposition to cancer or a response to a specific treatment,” said Kurzrock. “We look at everything about the patient—history, age, previous therapies, pathology results, tumor genomics and the immune system to find the best therapy for that individual.”

**PROSTATE CANCER**

Prostate cancer risk and consequences are highly variable, depending upon the tumor’s aggressiveness and the age and health of the patient. Personalized medicine in prostate cancer treatment is critical, said Christopher Kane, MD, chair of the Department of Urology.

“Some patients will live a lifetime and never be threatened by their prostate cancers. For them, we use active surveillance to monitor without treatment or until it is needed,” said Kane. “Others will experience metastasis and death within months or years of diagnosis. We need to understand each person’s disease to know their risks and treatment needs.”

Kane and colleagues are using an innovative restriction spectrum imaging/magnetic resonance imaging technology, combined with traditional ultrasound, to create a three-dimensional map of the prostate. The approach allows physicians to see high-grade or aggressive cancers that were previously undetectable.

“Until now, we’ve not had this [imaging technology] for the prostate,” Kane said. “We had to biopsy the entire prostate in an organized way. For many men undergoing biopsy, we missed aggressive cancers. Now we can really hit the mark on each individual.”
Chemists, biologists, engineers and many other UC San Diego researchers are already lining up with James McKerrow, MD, PhD, the new dean of Skaggs School of Pharmacy and Pharmaceutical Sciences – *literally*.

**MCKERROW BECAME THE SECOND DEAN OF SKAGGS IN JULY 2014.** One of his first initiatives was to build a formal drug development pipeline – a clearly delineated series of steps necessary to translate basic lab discoveries into potential new medicines and, ultimately, test them in human clinical trials. McKerrow lined up researchers to provide the resources and expertise at every step.

A drug development pipeline takes a discovery along a highly coordinated “conveyor belt” of tinkering and testing. Along the way, a project is touched by many experts, including biologists making discoveries in cells, chemists making new compounds, computer scientists building drug design models, and pharmacologists testing for toxicity and optimizing drug delivery.

“We already had all the drug development resources and talent, plus a very collaborative spirit,” McKerrow said. “We just needed to streamline them into a single, easy-to-use system.” The new drug pipeline launched earlier this year with a call for proposals.
McKerrow plans to use the pipeline and a new high-throughput, robotic screening center to develop novel therapies, including some aimed at tropical infectious diseases—a particular focus of his lab. He said the significant investment of resources is necessary because pharmaceutical companies lack financial incentives to develop new drugs for diseases that predominantly affect underdeveloped regions of the world.

“It’s the duty of a public university like us to fill this gap,” he said, “to work toward new diagnostics, vaccines and drugs that millions need but nobody is making.”

Research, of course, is just part of the Skaggs mission. McKerrow and Skaggs faculty are also charged with teaching and training approximately 240 PharmD students, 60 PhD students and 30 pharmacy residents each year.

These days that covers a lot of territory. New generations of pharmacists will be a different kind of primary health care provider. In 2014, California became the fourth state to allow pharmacists to initiate and monitor a patient’s drug therapy, rather than simply fill a doctor’s prescription.

As one of few pharmacy school heads with a medical degree rather than a degree in pharmacy, McKerrow is well positioned to lead students and trainees through this transition. He and faculty are working with the School of Medicine to evolve their curricula and better prepare pharmacy students for patient interactions and communicating with other members of a patient’s health care team.

“Soon doctors will be able to focus more on diagnosis, treatment launch and prognosis, while pharmacists will evaluate therapeutics and monitor patient medications over time,” McKerrow said. “That will ultimately be better for everyone. Doctors will be able to spend more time with their patients, while patients will discuss their therapeutic options, receive drug instructions and learn about possible side effects from a therapeutic expert—the pharmacist.”

James McKerrow, MD, PhD

“It’s the duty of a public university like us to fill this gap—to work toward new diagnostics, vaccines and drugs that millions need but nobody is making.”
Skaggs School of Pharmacy Dean James McKerrow says future pharmacists will have a long reach.

Rather than simply filling a doctor’s prescription, new generations of pharmacists will be a different kind of primary health care provider.
ONCE UPON A TIME, not all that long ago, actually, all a doctor could know about a patient’s tumor was where it originated – in the lung or breast, for example. Then the doctor would recommend a course of treatment: surgery, radiation or chemotherapy, and hope for the best.

The harsh reality, however, is that most therapeutic drugs only work in 15 to 20 percent of patients.

To improve cancer therapy – indeed, the treatments of many diseases – researchers are beginning to match patients with the best medicines, based on their unique genetic profiles. It’s called genomic medicine, or sometimes personalized or precision medicine.

Cancer is the poster child for genomic medicine, since in many ways it is a disease of the genome. At Moores Cancer Center at UC San Diego Health, doctors are sequencing the genomes of patients’ tumors and, based on that information, recommending the best treatments.

But genomic medicine isn’t yet routine for every patient, and certainly not for most diseases. Even if it were, the specific way a person’s genetic mutations actually cause disease remains unknown for most complex conditions. What’s more, that genetic information isn’t helpful unless there’s also a way to compensate for the mutations that produce the disease.

CONNECTING GENES TO DISEASE AND TREATMENT

“Affordable next-generation gene sequencing gives us the important genes, which is like revealing all the dots in a game of ‘connect the dots,’” said Trey Ideker, PhD, professor of medicine and bioengineering and division chief of medical genetics. “What we need now is to draw the links between those dots.”

That’s where the Institute for Genomic Medicine (IGM) comes in. The IGM, led by Kelly Frazer, PhD, brings together 25 faculty members, their research labs and an abundance of cutting-edge technologies – things like high-throughput gene sequencers, digital technologies and array-based platforms.

IGM’s goal is to unravel the genomic underpinnings of human health and disease and to translate those discoveries into new preventive and therapeutic medicines. To do this, IGM makes genomic technology accessible to all UC San Diego researchers, as well as outside customers.

While many scientists are using IGM’s resources to develop treatments tailored to individual patients, Ideker thinks there’s a bigger picture. Sure, no two people or tumors are genetically identical, but, as a systems biologist, Ideker said, “While unique themselves, many genetic mutations can be grouped by the downstream effects they have on a cell’s function.”

In other words, if gene A is in the same social network as genes B, C and D, a mutation in any of the four could lead to the same type of cancer. If that’s true, researchers hypothesize patients with mutations in any of those genes might share a similar diagnosis, prognosis and response to treatments.

COLLABORATION AND DATA SHARING

According to Frazer, personalizing medicine – to either individuals or subgroups – will require collaboration and sharing of data.
“Genomic science always has been and continues to be largely made up of individual labs contributing to larger projects,” she said. “Many IGM researchers are participating in these projects. Figuring out how to incorporate these data and make them fully available to the scientific community is a very important part of what the IGM is trying to accomplish.”

One example is The Cancer Genome Atlas (TCGA), an ongoing nationwide, multi-institution effort to sequence more than 500 tumor genomes, along with each person’s non-cancer genome, for 20 different tumor types. IGM researchers are using TCGA data to improve disease classification – subgrouping patients by the effects of their genetic variations – and search for new therapeutic targets.

Eventually, this information would feed back to clinicians at Moores Cancer Center and other medical centers.

Despite challenges, genomic medicine has come a long way in a short time – and continues to advance quickly. “Ten years ago, we couldn’t even sequence the human genome,” said Frazer. “Five years ago, we started talking about genomic medicine. Now we’re actually doing it. I think we’ll be just as amazed at what we’ll be doing five years from now.”

Researchers are beginning to match patients with the best medicines, based on their unique genetic profiles.
Farming practices may be driving windborne cause of heart problems in children.
The symptoms of Kawasaki disease (KD) are tell tale: high fever, rash, swollen feet and hands, cracked lips, and “strawberry tongue.” The disease – an inflammation of arterial walls – generally appears before the age of five.

KD is the leading cause of acquired heart disease in children, but in 95 percent of cases it can be effectively treated with intravenous immunoglobulin therapy and high doses of aspirin.

Cases along the east coast of the United States, meanwhile, appear to be associated with a Midwestern agricultural source.

“The disease could literally be blowing in the wind,” said Jane C. Burns, MD, professor and director of the Kawasaki Disease Research Center at UC San Diego School of Medicine and Rady Children’s Hospital-San Diego. “All the data point to an anthropogenic source, related to farming practices, and we are trying to prove it.”

Burns, who has been studying KD since her medical residency, and colleagues are scouring the air above Japan during the KD season, which peaks in December-January and June-July. They are looking for a causative agent that is toxic, abundant and lightweight enough to transit the Pacific Ocean on wind currents.

The most likely “Agent X” is an abundance of yeasts in the genus *Candida*, first discovered hovering two and three kilometers above Japan in the 2011 KD season.

A LOT IS KNOWN ABOUT KD. WHAT REMAINS UNKNOWN IS THE SOURCE OF THE DISEASE, which first emerged in Japan after World War II and now has global reach.

UC San Diego School of Medicine researchers are getting close to an answer. Moreover, they are developing new imaging technologies and therapies to reduce morbidity and mortality in patients who do not respond well to traditional therapies and face a heightened risk of heart attack.

In Japan, KD affects 298 in 100,000 children younger than the age of five. In the United States, the comparable figure is 22 in 100,000. The mortality rate from KD is less than 1 percent, but this does not account for deaths among adults who sustained coronary artery damage from childhood KD.

In recent years, UC San Diego physicians and climate scientists at Scripps Institution of Oceanography, in collaboration with Spanish and Japanese colleagues, have linked cases of KD in Japan, Hawaii and the western United States to wind patterns originating over a major cereal-growing region in northeastern China.

The most likely “Agent X” is an abundance of yeasts in the genus *Candida*, first discovered hovering two and three kilometers above Japan in the 2011 KD season. No toxin has yet been identified in association with the airborne fungi, but in mouse models of the disease predating the 2011 discovery, it was found that injecting animals with *Candida* components induced coronary damage.

Just over 16 percent of China, roughly 3.7 billion acres, is cultivated land. Among primary crops are rice, wheat, sorghum, peanuts, tea, millet and barley.
Symptoms of KD:
Fever lasting at least 5 days
Swollen, red, cracked lips and tongue
Swollen, red feet and hands
Swollen lymph nodes in neck
Red eyes
Body rash

“KD is not transmitted person-to-person,” said Burns. “It doesn’t respond to antibiotics, so a bacterium is unlikely. Climate data suggest that symptoms appear within hours of contact with Agent X, which makes a virus less likely. This all points to a toxin – and fungi are famous for producing toxins.”

The rub is that there is no KD hot spot in the putative source region in China. In fact, the incidence rate among children in this area is lower than in Japan.

Genetics offers a partial explanation. Boys of Asian, Pacific Island and African-American heritage are more susceptible to the disease; and among Asians, Japanese and Koreans are more predisposed than Chinese.

Another possible factor: Agent X may need to be exposed to atmospheric chemistry to become dangerous.

HEART DISEASE LATER IN LIFE
Researchers plan to analyze an existing year-round, long-term record of aerosol samples collected over a peninsula in Japan that is the first point of contact with northwesterly winds from China. A study of this time series might reveal seasonal changes in the composition of microbes or other potential environmental molecules that could help solve the KD mystery.

Burns is also collaborating with Lucila Ohno-Machado, MD, PhD, chair of the Department of Biomedical Informatics, on a whole-genome sequencing of a San Diego family in which two children have had KD and two have not.

Burns and Adriana Tremoulet, MD, associate professor of pediatrics, also have two ongoing clinical trials to investigate whether a rheumatic arthritis medication and a statin might be able to help children who do not
Boys develop KD almost twice as often as girls. Average age of diagnosis is 2. Without treatment, roughly one-quarter of affected children will subsequently develop heart disease involving the coronary arteries.

respond to standard KD treatment. These children are at particularly high risk of having heart problems later in life.

In one study, led by Lori Daniels, MD, director of the coronary care unit at Sulpizio Cardiovascular Center at UC San Diego Health and associate professor of medicine, approximately 5 percent of adults age 40 and younger who were evaluated for coronary ischemia (lack of blood flow to the heart) showed signs of KD-inflicted heart damage.

To improve screening of these patients, Andrew Kahn, MD, PhD, associate professor in the division of cardiology, has pioneered the use of low-radiation computed tomography (CT) scans to detect calcium deposits in the coronary arteries, indicative of long-ago damage from KD.

“The goal is to identify patients at risk of heart problems and have them followed by cardiologists for continued monitoring and care,” he said.

Alison Marsden, PhD, a mechanical engineer at UC San Diego Jacobs School of Engineering, is using these CT scans to construct individualized simulations of blood flow through a patient’s heart. The simulations identify places where blood flow stagnates and might form clots.

“Clinicians use an artery’s diameter as the metric for deciding whether to prescribe an anticoagulant,” she said. “Our early results suggest predictive modeling of blood flow may be a better means of calculating blood clot risk. Our hope is that blood flow simulations through a computer model of a patient’s heart can provide doctors with the information they need to decide how to best treat their patients.”

The Kawasaki Disease Research Center is a joint collaboration of UC San Diego School of Medicine, Scripps Institution of Oceanography and Rady Children’s Hospital-San Diego. Help find a cure by giving online at giving.ucsd.edu or calling 858-822-4562.
A New Olden Age

As demographics skew older, UC San Diego center offers a vision bolder

“THERE’S AN UPSIDE TO GETTING OLDER,” quips Dilip Jeste, MD, the first associate dean for healthy aging and senior care at UC San Diego School of Medicine: “Your old clothes are back in style. All your enemies are dead. One martini does the work of three.”

There’s a serious side too: the growing, pressing need to improve and promote the long-term health and well-being of older Americans. This is a passion of Jeste’s, and his mission as director of the Center for Healthy Aging and Senior Care is for the center to become a force in the national conversation about how society can transform what is perhaps disparagingly dubbed the “silver tsunami” into a “golden wave.”

“We’re on the cusp of an amazing phenomenon,” said Jeste, who is also Distinguished Professor of Psychiatry and Neurosciences and director of the Sam and Rose Stein Institute for Research on Aging. “Over the next few decades, the country’s older population will almost double, from 43 million in 2012 to nearly 84 million by 2050.”

The graying of America presents myriad challenges and opportunities, which is why Jeste said entities like the Center for Healthy Aging are needed. “Initially, we’ve been focusing on health and health care for older adults. But healthy aging needs to be more than medicine, so we’re also examining issues such as technology, housing, transportation and urban planning. All of these things have major impacts on the well-being of seniors.”

ACTION ACROSS CAMPUS
Part of the UC San Diego School of Medicine, the Center is taking a multidisciplinary approach, seeking to break professional silos and bring together experts from across campus, plus reach out to government and industry leaders, local to national.

High on the list of early priorities is housing. “We’re going to see a revolution in senior housing,” said Jeste. “Aging boomers want to age in place. This will mean designing housing that helps older people remain in their homes.”

He predicts future senior housing will include a “health care room,” where seniors can see and talk with doctors through computer networks, with blood pressure and other vital signs monitored via wireless connectivity. “We don’t have enough health care professionals trained to treat the growing numbers of older adults. Technology will be absolutely critical in providing care to people in their homes.”

HOME ROBOTS AND EXERGAMES
Other envisioned technological innovations include robotics and electronics to transport seniors and, well, get them moving on their own. Driverless cars, for example, might serve when older individuals can no longer drive safely on their own. In-home computers could run exercise programs.

“I think future housing for seniors will be designed with activity rooms,” said Jeste. “With a simple console and a video ‘exergame,’ seniors can play virtual tennis, bowl or golf in their homes. It’s inexpensive, fun and can improve their health.” Indeed, in a 2010 study involving seniors suffering from mild depression, Jeste found that playing exergames for 35 minutes three times a week significantly improved mood, sense of well-being and overall cognitive performance.

“I think about the future for seniors like Tomorrowland at Disneyland,” said Jeste. “How can we make older people’s lives happier and the communities more senior-friendly? It’s an exciting time to be at UC San Diego, working with experts in so many different fields as well as the community to bring about innovative and transformative change in this area.”
Healthy aging is about more than medicine. It’s about housing, technology, transportation, urban planning and more – all impacting the well-being of seniors.

The newly established Center for Healthy Aging is poised to lead in its field. To learn more or make a gift, visit aging.ucsd.edu and click “GIVING” or call 858-822-4562.
Mitochondria are celebrated as the “power plants of cells.” In recent years, however, appreciation of mitochondria has dramatically broadened and risen, particularly in terms of what can happen when they do not do their many jobs well.

Mitochondria power cells, and when they fail, a lot of bad things can happen.
WHEN MITOCHONDRIA FAIL, THE CONSEQUENCES CAN BE IMMENSE, from neuromuscular disorders and various heart diseases to cancer, diabetes, developmental delay, chronic infections and premature aging.

Such heterogeneity long stymied a fuller appreciation of the scope of mitochondrial diseases, but that’s changing, due in large part to the work of physician-scientists like Richard Haas and Robert Naviaux.

In the mid-1990s, Haas, MD, professor of pediatrics and neurology, and Naviaux, MD, PhD, professor of medicine, pediatrics and pathology, launched the Mitochondrial and Metabolic Disease Center at UC San Diego School of Medicine, among the first of its kind in the world.

DIFFICULT DIAGNOSIS

Mitochondrial diseases are extraordinarily difficult to diagnose. An official diagnosis requires three or more organ systems to be deemed failing or a recognizable disease to be present but displaying atypical symptoms. “A decade ago, a patient might see 12 doctors before being diagnosed,” said Naviaux.

But as researchers began linking mitochondria to more processes and functions, such as immunity and inflammation, and frontline doctors became better educated about recognizing possible symptoms, the situation changed – for better and worse. “A correct diagnosis might happen now after just two or three doctors,” said Naviaux.

Mitochondrial disease is caused by genetic mutation, either inherited or spontaneous. The standard model blames oxidative stress due to reactive oxygen species (ROS), chemically reactive molecules that are a natural byproduct of metabolism. In healthy cells, ROS levels are rigorously controlled. When they rise too high, ROS can harm mitochondria, particularly if levels remain elevated.

Primary mitochondrial disease, which occurs when a mutation causes malfunction and symptoms, affects up to one in 5,000 people. Secondary mitochondrial disease, which requires both a genetic alteration and an external environmental force that triggers dysfunction, is even more common. Mitochondrial disease is typically a childhood disease, but adult-onset cases are increasing.

Current care involves dietary controls, support treatments, like physical and respiratory therapies, and the use of certain vitamins and antioxidants, such as Coenzyme Q10 and glutathione. These treatments may alleviate symptoms and preserve existing functions, mobility and strength, but they are not cures.

Conventional wisdom says mitochondrial dysfunction means the organelle is damaged, but Naviaux and others argue otherwise. “My view is that sometimes the machine – the cell – is simply working with a different set of instructions. That’s a lot different than saying damaged. It changes how you think about treatment.”

Specifically, Naviaux asserts that some mitochondrial or metabolic diseases may better be explained by his “cell danger theory.” It posits that cells threatened by environmental factors, such as ROS, pathogens or toxins, react defensively. Their membranes stiffen. Internal metabolic processes, most notably those of mitochondria, are altered. Communications close down. The result is a chronic condition or disease dictated by the type of cell affected. Autism is one example.

FAILURE TO COMMUNICATE

“Cells behave like countries at war,” said Naviaux. “When a threat begins, they harden their borders. They don’t trust their neighbors. But without constant communication with the outside, cells begin to function differently. In the case of neurons, it might be by making fewer or too many connections. One way to look at this related to autism is this: when cells stop talking to each other, children stop talking.”

In several recent papers, Naviaux has described experiments with mouse models of autism in which a century-old drug called suramin, used to treat human sleeping sickness, blocks cell danger signals, appearing to restore normal cell activity. Scientists report autism symptoms in treated mice disappear. They launched their first clinical trial this year.

Naviaux acknowledges it’s a big leap from mouse to human. Suramin itself will not be the solution. The drug’s benefits wane over time, and its side effects render it inappropriate for long-term use.

But Naviaux believes his research – and that of others – is broadening views about what constitutes and causes mitochondrial disease. He said his findings do not contradict prevailing research, but rather augment it and underscore the idea that mitochondrial diseases are enormously complex, with multiple risk factors.

“The goal is to upend therapeutics, to no longer simply treat the damage caused by the disease, but restore the healthy connections within the cell so that normal functions return and the cell can fix itself.”
Rising metabolic disease is a major cause of blindness
"We’re not just talking about people’s eyes, but their ability to work, their ability to drive. These people often also have kidney disease and heart disease. Diabetes affects their brains, and the circulation to their hands and feet."

Eric Nudleman, MD, PhD (pictured on right)
In 2014, the Sanford Stem Cell Clinical Center at UC San Diego Health launched three first-in-human clinical trials to evaluate the safe use of embryonic stem cells in patients with spinal cord injury, diabetes or blood cancer.

PEOPLE FROM AROUND THE WORLD LEARNED OF THE GROUNDBREAKING STUDIES through newspaper headlines, Google searches and word of mouth.

“When the stem cell trial for patients with diabetes was first announced, my email and voicemail were instantly flooded,” said Todd May, MS, clinical trial coordinator. “Within weeks, I had more than 1,000 inquiries from the United States and Australia, South America and Europe. The desire for those living with a chronic disease to pursue a cure, even by participating in a safety trial, is enormous.”

SAFETY COMES FIRST

May was on the frontline of helping screen potential matches for just a few spots in the Phase I diabetes study. The screening process included an in-depth, somewhat sobering, education on what it means to enroll in a safety study.

“You volunteer your time and self so that the study of the drug or device can proceed through testing,” he said. “If there is eventual FDA approval, you know you helped bring that therapy to market.”

For participants in Phase I studies, however, that help can mean a long haul. Studies may require follow-up clinic visits and testing, such as blood draws and radiology scans, for up to five years.

Clinical trials volunteers are critical to moving science forward

Photographs by David Altenholz and Ryan Parks
PAYOFF OVER TIME

“In the beginning, the participants are excited because there is a high hope factor, especially for stem cells;” said May. “In a typical trial, though, as time progresses it can be tough to keep going. You have to continuously remind the participant of why the trial is occurring. You come back to the statement, ‘You may be helping people in the future with the same condition. It could be a family member or even your children.’”

Michael Kalichman, PhD, director of the UC San Diego Research Ethics Program, said it’s unlikely that goodwill alone motivates participants in safety trials. “Initially it may appear that participants enroll for purely altruistic reasons, but that’s usually not the case. It’s more of a leap of faith,” he said. “Researchers need to be very sensitive to the state of mind of the potential participant. When patients are sick with a chronic condition, they are more likely to opt into a trial if they feel they have no other choices. It’s hard to turn away from something that is promising.”

Kalichman, the Sanford Stem Cell Clinical Center and the Institutional Review Board at UC San Diego act in concert to ensure both the safety of the trial and the mindset of the volunteers. “When we invite the public to participate in a safety study, it is our ethical obligation to be as clear as possible about what it means to enroll,” said Kalichman.

“‘The education is not a one-shot deal. It’s not the one-time signing of paperwork. It needs to be a recurring conversation. Informed consent is not a document, it’s a process:’

DEMANDS OF GOOD SCIENCE

Mark Lawson, PhD, is chair of the UC San Diego Embryonic Stem Cell Research Oversight Committee. The group ensures the provenance and authenticity of stem cells used in UC San Diego trials. He points out that whether it’s altruism or self-interest, clinical trials volunteers are critical to moving science forward.

“A powerful psychological interaction takes place when a person decides to participate in a trial. Clearly communicating the potential risks and benefits is key to maintaining the public confidence so that these trials will continue to progress. Think of the first person who stepped up to test the first polio vaccine,” said Lawson. “They changed the world. Where would we be if those first participants did not come forward? They contributed to something not for themselves, but for those in the future. This trust should be rewarded with honesty and good science.”
Highlights

2015

1. FRIEDMANN WINS JAPAN PRIZE
Theodore Friedmann, MD, professor in the Department of Pediatrics, was named one of three recipients of the 2015 Japan Prize, a prestigious international award honoring laureates whose “original and outstanding achievements in science and technology have advanced the frontiers of knowledge and served the cause of peace and prosperity for mankind.” Friedmann was recognized for his pioneering research and contributions to the development of gene therapy.

2. NEWLY NAMED SHILEY EYE INSTITUTE
Reflecting its emergence as a regional hub for unparalleled clinical care, research, education and community service, the Shiley Eye Center was renamed the Donald P. and Darlene V. Shiley Eye Institute at UC San Diego Health, encompassing the Shiley Outpatient Surgical Center, the Anne F. and Abraham Ratner Children’s Eye Center, the Hamilton Glaucoma Center, and the Joan and Irwin Jacobs Retina Center.

3. UC SAN DIEGO GOES TO MALAYSIA
UC San Diego and Perdana University in Malaysia announced plans to collaborate on further development of the Perdana University Graduate School of Medicine. The 10-year partnership will focus on enhancing and implementing a forward-thinking medical curriculum, a model for comprehensive patient care, and a platform for innovative world-class research in Malaysia and Southeast Asia.

4. MESIROV AND SALTIEL COME TO UC SAN DIEGO
Leading computational biologist Jill P. Mesirov, PhD, (pictured) joined the School of Medicine and Moores Cancer Center as associate vice chancellor for computational health sciences and professor of medicine. Mesirov will help formulate an overarching strategy for computational health sciences and research computing. Previously Mesirov was at the Broad Institute of MIT and Harvard University.

Alan Saltiel, PhD, one of the country’s top researchers in metabolic disorders, joined faculty as a professor in the Department of Medicine and will head the new comprehensive diabetes center, unifying basic science and clinical efforts. He previously served as director of the Life Sciences Institute at University of Michigan.
5. VASSILIADIS AND RADY GIFTS

More than 1,000 donors have contributed a total of $144 million to the new Jacobs Medical Center at UC San Diego Health, opening in 2016. This includes $100 million in contributions from Joan and Irwin Jacobs. Among more recent gifts: $8.5 million for the advanced surgery floors from Carol Vassiliadis and a $12 million gift from Evelyn and Ernest Rady (pictured) for women and infants services.

6. DIGITALLY DISSECTING A CANCER CELL

Researchers at UC San Diego, UC San Francisco and elsewhere launched the Cancer Cell Map Initiative, an ambitious and unprecedented effort to determine how all of the components of a cancer cell interact.

Micrograph by Thomas Deerinck

7. LIVE LONG AND MEASURE

Seeking to boldly go where medical science has not gone before, Clinical and Translational Research Institute (CTRI) is the official testing site for the $10 million Qualcomm Tricorder XPRIZE, a global competition to develop a consumer-friendly, mobile device capable of diagnosing and interpreting 15 physiological conditions and capturing vital health metrics. The XPRIZE competition is inspired by the tricorder medical device used in Star Trek. Final results will be announced in 2016.

8. CTRI EARNS MAJOR NIH GRANT

CTRI received its second major Clinical and Translational Science Award from the National Center for Advancing Translational Sciences, part of the National Institutes of Health. The five-year grant, one of the largest, single NIH grants in campus history, will help accelerate development of clinical trials, particularly in the use of big data. The new Altman CTRI building is slated to open in 2016.

Rendering by ZGF Architects LLP

9. WERB WINS INAUGURAL AVENIR AWARD

Dan Werb, PhD, an epidemiologist and visiting postdoctoral scholar in the Division of Global Public Health, was named one of four recipients of the first Avenir Award, a $1.5 million research grant from the U.S. National Institute on Drug Abuse. Werb specializes in the fields of HIV, addictions and drug policy.
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, the region's only academic health system.

discoveries.ucsd.edu