The only quote author and physician Abraham Verghese, MD, keeps framed in his bedroom is from a 16th-century physican named Paracelsus: “This is my vow: to love the sick, each and all of them, more than if my own body were at stake.”

As the keynote speaker at the School of Medicine commencement on June 14, Verghese, addressing a crowd gathered under a large white tent on Alumni Lawn, asked the graduates to respect the timeless rituals of medicine. A champion of hands-on medicine, he cautioned graduates against letting technology push them too far from the patient’s bedside. “Look to the time-honored role of the physician-patient connection, and learn from this relationship, he advised.

“Whenever you enter a [patient’s] room, be conscious of that legacy, of this unbroken chain extending back centuries — how in standing before a patient, you stand there as the latest incarnation of this lineage, and you have behind you generations of physicians … from Paracelsus, Osler, Curie, Shumway,” said Verghese, who is also the senior associate chair for the theory and practice of medicine in the Department of Medicine.

Dressed in caps and gowns, the graduates celebrated the occasion by applauding their own years of hard work; thanking family, friends and faculty; hugging their classmates; and, for some, accepting diplomas in one hand while holding a baby in the other.

Guy Haskin Fernald, who earned a PhD, drew laughs and applause as he crossed the stage to accept his diploma with four children in tow. “Way to go, Dr. Leon!” someone yelled from the crowd, as Leon Castaneda, who earned an MD, cheerfully accepted his diploma.

In the 2013-14 academic year, 71 students earned PhDs, 84 earned MDs, 54 earned master’s degrees, and one earned a joint MD/MS degree. The ceremony began with Dean Lloyd Minor, MD, introducing Verghese, the Linda R. Meier and Joan F. Lawn, who earned a PhD, who had performed the first successful human liver transplant on a man with acute liver failure who had come to the hospital in a deep coma. The operation went well. Two days later, the patient awoke.

The School of Medicine commencement took place June 14 under a tent on Alumni Lawn. The ceremony marked years of hard work by graduating students.

The new findings, published June 19 in Cell, may throw light on psychiatric disorders marked by impaired social interaction such as autism, social anxiety, schizophrenia and depression, said the study’s senior author, Karl Deisseroth, MD, PhD, a professor of bioengineering and of psychiatry and behavioral sciences. The findings are also significant in that they highlight how brain activity controls complex behavior. A combination of cutting-edge techniques developed in Deisseroth’s laboratory permitted unprecedented analysis of how brain activity controls behavior.

Deisseroth, the D.H. Chen Professor and a member of the interdisciplinary institute Stanford Bio-X, is a practicing psychiatrist who sees patients with severe social deficits. “People with autism, for example, often have an outright aversion to interact socially. Stimulating this circuit — one among millions in the brain — instantly increases a mouse’s appetite for getting to know a strange mouse, while inhibiting it shut down its drive to socialize with the stranger.”

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The story behind new Stanford Medicine website

An effective online presence is a key element of any organization’s ability to engage with people around the world. Most people now form their first impressions of a brand through a digital lens. They assume that innovative, pre-eminent organizations have well-designed, relevant and easy-to-use websites.

Stanford Medicine needed to have a website that reflects the pre-eminent nature of our people, our work and our outcomes in health care, research and education. This ability to inspire can have as much of an impact on our external audiences as on our internal community of faculty, students and staff and our shared sense of purpose.

More than two years ago, we started refreshing our understanding of what role the Web plays, and could play, as a resource for the various types of organizations within Stanford Medicine, whether an institute, department, research center, training program or initiative. We formed a team from across the school to guide the initial concept for our new design and platform. Over the last several months, Pam Lowney, our senior Web strategist, led an effort to engage with faculty, staff, students and our hospital counterparts to help shape and evaluate the overall effectiveness of our new navigation and user experience.

Visually, the new website is quite striking. How does it make it easier to view content and navigate the site?

The new site works well across the multitude of devices that we all carry. The site layout changes automatically to accommodate small screens, such as those for phones and tablets, and large screens. The platform dynamically adapts in delivering the correctly sized images, audio and video so that mobile experiences are faster.

Our new Web system also represents a complete transformation in how individual sites are built and maintained. The publishing engine functions largely as a drag-and-drop tool that can be accessed from a standard browser. The Web publishers in individual units will be able to quickly create custom layouts filled with rich-text and multimedia elements that will help them effectively showcase their content. The component library available to our Web publishers currently includes text editors, banners, image boxes, tables, feature panels, video players, an audio player, social network embeds, news and profile lists, timelines, buttons, forms and more. Everything you need to build a site is available without having to code anything in any software. We’ll continue to enhance all of these tools and offer more over the coming months.

The school’s website is pretty vast, and this initial launch covers only the top-level pages. How long will it take for all of the school’s Web Pages to be integrated into the new environment?

Yes, the Stanford Medicine website environment includes hundreds of sites. The initial phase established the foundation and the top landing pages, the news center and a handful of smaller sites. In our next phase, which has already kicked off, we will assist with the migration of about 200 formal academic and program sites. These sites have been identified, and we have scheduled these migrations with the site owners. In parallel, we are training all of the Web authors for these sites.

Later this summer we will also turn on the capability to do manual migrations for publishers who want to move to the new site as soon as possible. We plan to continue with the assisted migrations after this first migration phase is complete.

What kind of feedback are you getting? If people spot problems, what should they do?

We have been hearing from all across Stanford Medicine that the design is compelling and interesting. But the biggest feedback is that the design represents our mission well. Publishers love the ease of the use of the new system and are very excited to start using this new site for their online communications.

As for problems, it is inevitable that you run across scenarios that you could not test. We’ve run into some broken links that we’ve quickly resolved as they are reported, but the site has been hugely available and performing well in the first few days. If people spot any defects, the best way to get help is by using our online service desk at http://med.stanford.edu/irt/help. I read all of the comments and route them to the appropriate people.

We also get ideas for how we can make the Web environment even better. We like that feedback because one sobering truth about the Web is that we are never done. Expectations, standards and capabilities change daily, so we can’t make the Web a new foundation to an even higher level of excellence.

Blood test identifies heart rejection earlier than biopsy can

By Krista Conger

Stanford researchers have devised a noninvasive way to detect heart-transplant rejection weeks or months earlier than previously possible. The test, which relies on the detection of increasing amounts of the donor’s DNA in the blood of the recipient, does not require the removal of any heart tissue.

“This test appears to be safer, cheaper and more accurate than a heart biopsy, which is the current gold standard to detect and monitor heart-transplant rejection,” said Stephen Quake, PhD, professor of bioengineering and of applied physics. “We believe it’s likely to be very useful in the clinic.”

Quake, the Lee Otterson Professor in the School of Engineering and a Howard Hughes Medical Institute investigator, is a senior author of the study, which was published June 18 in Science Translational Medicine. The other senior author is Mark Khush, MD, assistant professor of medicine, and the lead author.

The test, called a cell-free DNA test, is different from another blood test, AlloMap, used to detect rejection. The commercially available AlloMap test takes a blood sample to analyze the expression of immune-system genes involved in rejection. The researchers found the cell-free DNA test outperformed AlloMap by a substantial margin.

“We’ve found that this cell-free DNA assay is a very accurate way to diagnose acute rejection, sometimes weeks to months before a biopsy picks up any signs,” Khush said. “This earlier detection may prevent irreversible damage to the transplanted organ.”

Participants with signs of rejection can be placed on anti-rejection medications to mitigate the body’s attack on the system’s attack. Sometimes, however, the rejection episode is too late and a second transplant is required.

Currently, heart-transplant patients undergo dozens of heart biopsies the first year after transplant and years after their transplant. During a biopsy, a small tube is threaded through the jugular vein in the neck, and a small pincer is used to pluck off small bits of heart tissue for analysis. The procedure is uncomfortable and may cause damage to the transplanted organ.

The new website features a modern, flexible design system and publishing platform.

Mark Trenchard
A new study led by investigators at the Stanford School of Medicine has implicated a new type of endocannabinoid — a neurotransmitter that regulates pain, inflammation and cell death — in the early stages of Alzheimer’s disease.

In the study, published June 18 in Neuron, Madison and his colleagues analyzed A-beta’s effects on a brain structure known as the hippocampus. In all mammals, this mid-brain structure serves as a combination GPS system and memory-filing system, along with other duties.

“The hippocampus tells us where we are in space at any given time,” said Daniel Madison, PhD, associate professor of cellular physiology and a co-author of the new study, is now chief officer for translational research at Stanford Health (a joint administrative body of the School of Medicine and the School of Engineering, and jointly administered by the School of Medicine and the Hughes Medical Institute).

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that has become the nature of our work,” he said. “You will need courage and de-
termination to push back when things detrimental to your time and your care of
the patient are being thrust at you. Electronic medi-
cal records don’t take care of patients: You and our
amazing colleagues in nursing and the other health-
care professions care for

People take care of
other people,” he said to
loud and long applause
from the audience.

Both heritage and ritu-
als, like the ritual of com-
encement, play an important role in
the career of a physician, he said.

“You are also participating in a time-
less ritual... when you get to examine a
patient. You are in a ceremonial white
gown. You stand there not as yourself,
but as the doctor. As part of that rit-
ual they will allow you the privilege of
touching their body, something that in
any other walk of life would be consid-
ered assault.

“The ritual properly performed earns
you a bond with the patient... The rit-
ual is timeless, and it matters.”

Verghese also said that he had learned
innumerable lessons from his patients,
and he went on to share one.

“I had a patient who was a hemo-
ephilic. He was a col-
lege teacher in his 30s
when I met him. He
walked with a stiff
gait, his arms swinging at an odd angle
at his side, the result of many episodes
of bleeding into his joints when he was a
child. The child his family had more hospital
admissions than most children had ice
cream.

The patient survived childhood, only
to be infected by the AIDS virus in the
1980s from his many blood transfusions.

“He was uncommonly brave and dealt
with AIDS matter-of-factly. Once, to-
ward the end of his life, I put him in hos-
pital — he hated to be admitted. I had
no treatment that would reverse things,
we had nothing to offer him that night, no
way to minister to him. In fact, he was
ministering to me, he was instruct-
ing me.”

The patient told Verghese that as a
little boy, he would sometimes wake up
in the night with pain in a joint. He
knew that he was bleeding into the joint,
but he also knew that his parents badly
needed their sleep — they were each
working two jobs, working weekends. If
he woke them, they would dutifully get
up and sit with him, put ice packs on his
joints and take him in the morning to
the hospital. So he did his best not to wake them,
to wait till morning so they could get
some sleep.

And his way of toughing it out was
to put a record on his toy record player,
a hymn called Joy Comes in the Morning,”
Verghese said. “He would play that again
and again until dawn broke. That was his
way of coping, his mantra for carrying
on. He is long dead, but in my tough-
est times, that is what I fall back on, my
memory of him, his courage, his sto-
icism, and telling myself to hang in there,
because joy comes in the morning.

“Graduates of the Class of 2014, may
you celebrate the rituals of medicine,
recognizing their im-
portance to both you
and the patient. ... May you find coun-
tage to face your own
personal trials by
learning from your
patients’ courage....

“When you come on rounds to see
your patients, may your presence bring
joy in the morning. It has been a privi-
lege to watch you on your journey. Good
luck and Godspeed.”

After the ceremonies, graduates
bugged family members and friends,
then discarded their ceremonial robes
in the “regalia return bin” and headed to
lunch on the Dean’s Lawn.

“I’m just really excited,” said Hiwot
Araya, a new MD, who invited 20 mem-
bers of her family from Ethiopia, all of
whom were excited to see Verghese, a na-
tive of Ethiopia himself who writes often
about the country.

“This graduation is different than un-
dergrad. More intense. Many of us start
work on Monday,” said Araya, who was
set to begin an internship in internal
medicine at UCLA.

“Dr. Verghese is an amazing speaker,”
said Jaimie Henderson, MD, a profes-
sor of neurosurgery and of neurology
and neurological sciences, chatting with
a woman in a wheelchair after the cer-
emony. “Listening to him it’s like, ‘Yeah,
that’s why I’m a doctor.’”
Awards honor exceptional work in education and patient care

At the School of Medicine’s commencement June 14, more than three dozen faculty members, students, trainees, staff and affiliated staff were recognized for dedication to and excellence in graduate and medical education, patient care and teaching.

DAVID VEC, MD, clinical instructor of medicine; LESLIE LEE, MD, clinical associate professor of neurology and neuroscience; and DANA TRAUTMANN, MD, clinical assistant professor of medicine were honored with the Arthur L. Bloomfield Award for Excellence in Teaching at the Palo Alto VA. Frederick was chosen by faculty, students and full-time faculty members.

MARINA BASINA, MD, clinical assistant professor of medicine, was honored with the Alwin C. Rambarr-James B.D. Mark Award for Excellence in Patient Care, which recognizes a member of the medical faculty for his or her service to patients and their families, excellence in providing medical treatment, and effectiveness and compassion in interactions with patient-care staff. The award was established in 1985 to honor the late Dr. Mark, a Chicago pediatrician long associated with the medical school and was renamed in 1997 to include Mark, MD, a Stanford thoracic surgeon and professor emeritus who was Rambarr’s son-in-law.

GILBERT CHIH, MD, PhD, professor of medicine and of biochemistry, received the Lawrence H. Mathers Award for Exemplary Commitment to Clinical and Active Involvement in Medical Student Education. The award, which was created in memory of the late Mathers, MD, PhD, professor of pediatrics and of surgery, recognizes an individual who exemplifies the values and achievements of Mathers’ work and life.

JAMES LAU, MD, clinical associate professor of surgery; received the Learning Environment Faculty Award.

MADAKI BRYANT, education manager at the School of Medicine, received the Medical Education Service Award.

DONALD REGULA, MD, professor of pathology, was recognized with the Outstanding Service to Medical Education Award.

JENNIFER ANDREWS, MD, clinical assistant professor of pathology and of pediatrics, received the Outstanding Lecture/Presentation Award.

MALIKA KHERAJ, MD, received the Outstanding Community Clinic Preceptor/Preceptorship Instruction Award.

AUDREY KUANG, MD, received the Outstanding Community Clinic Preceptor/Preceptorship Instruction Award.

MARIKO BENNET, an MD/PhD student, received the Teaching Assistant Award.

Faculty awards in graduate education

MIRIAM GOODMAN, PhD, associate professor of molecular and cellular physiology; TIM METES, MD, PhD, professor of genetics; Aaron Straight, PhD, associate professor of biochemistry; TONY CLANDANNIN, PhD, associate professor of neurobiology; THEODORE JARDESTZKY, PhD, professor of structural biology; SHERRI KRAMBS, MD, PhD, associate professor of surgery; DAVID SCHNEIDER, PhD, associate professor of microbiology and immunology; MAY BETH MUDGETT, PhD, associate professor of medicine; and JENNIFER RAYMOND, PhD, associate professor in molecular and cellular physiology; MARGARET FULLER, MD, professor of genetics; and DAVID KINGSEY, PhD, professor of developmental biology earned the Excellence in Teaching Award in recognition of their group effort to develop and implement an innovative and closely mentored experience for PhD students as they entered their training in the biosciences.

ANTHONY RICCI, PhD, professor of otolaryngology; MARY BETH MUDGETT, PhD, associate professor of biology; and JENNIFER RAYMOND, PhD, associate director of neurobiology received the Excellence in Diversity Award, which recognizes faculty who made distinguished contributions toward enhancing diversity, equity and inclusion across the biosciences.

Henry J. Kaiser Family Foundation awards

ERROL OZDALAGA, MD, clinical assistant professor of medicine, earned the Kaiser Family Foundation Award for Outstanding and Innovative Contributions to Medical Education.

JAMES FANN, MD, professor of cardiothoracic surgery; SAIFAN JARADHE, MD, professor of neurology and neurological sciences; and JAMES LAU, MD, clinical associate professor of surgery, received the Kaiser Award for Excellence in Clinical Teaching.

ERIC STRONG, MD, clinical assistant professor of medicine; JONATHAN BERNSTEIN, MD, PhD, assistant professor of pediatrics; and CHRISTOPHER GONZALEZ, MD, clinical assistant professor of pathology, earned the Kaiser Foundation Award for Excellence in Preclinical Teaching.

Gold Foundation Award

The Arnold P. Gold Foundation Award for Humanism and Excellence in Teaching recognizes medical residents for their dedication to and compassion for medical students. This year’s recipients were JON LIEBERT, MD, surgery; JON METES, MD, biochemistry; KENDRICK CARL, MD, internal medicine; CHAD MCCARTHY, MD, pediatrics; LINDSAY WHEELER, MD, of genetics and gynecology; and LOUISA WEN, MD, anesthesiology.

Method for observing kinase function in cells could speed drug discovery

By Tom Abate

Think of the human body as an intricate machine whose working parts are proteins: molecules that change shape to enable our organs and tissues to perform tasks such as breathing or eating or thinking. Of the millions of protein types, 500 in the kinase family are particularly important for communication among the body’s tissues since they regulate cell signalling, which is something no one else has ever seen," said Markus Covert, PhD, an assistant professor of bioengineering and senior author of a paper, published online June 19th in Cell, that describes the findings.

“Cancers can occur when a kinase inappropriately tells a cell to ‘grow, grow, grow,'” Covert said. “The reverse can also be true, if a cell reaches what should be the end of its normal life-span but the kinase never says ‘die, die, die.'”

Using the new technique, researchers could observe and compare kinase activity in healthy versus diseased cells. While both healthy and diseased cells, then introduce an experimental drug to see how it affects the living cell.

Prior to this, researchers would have had to pulverize a cell sample, extract the kinase proteins, and then implement an innovative and closely mentored experience to observe any changes that result in that same cell sample.

Covert believes that this process will speed the development of new drugs aimed at cancers and other conditions linked to kinase irregularities.

The new method technique enables researchers to read the activities of multiple kinases in living cells, and if they administer an experimental drug to a cell culture, the kinase will pulverize this sample and sift out the data on kinase activity.

Sergi Regot, PhD, a postdoctoral scholar in Covert’s lab, spent more than a year developing and refining the process that he outlined as the lead author of the Cell paper.

It all begins with a conceptual understanding of how kinase messenger proteins transmit signals.

Protein signaling is a complex cascade of physical events inside a cell. The protein itself is a long chain of atoms. Different groups of atoms in the chain perform different functions. Some atoms serve as the antenna or receiver that directs the kinase to a specific location. Upon arriving at its destination, the kinase delivers its message, instructing the protein to do something inside the cell.

The kinase essentially has two parts: One part finds the address inside the cell, and the other part delivers the message.

To track the activity of this signaling system in living cells, Regot came up with the idea of creating a fake destination for the kinase. He called this decay a kinase Translocation Reporter, or KTR. He tagged the KTRs with a fluorescent protein so he could track their locations inside the cell with special microscopy tools. He added one other crucial element to the KTR, a molecular switch that indicated whether the kinase was active or inactive.

“All of this was easier thought of than accomplished, but in the end we did it,” Regot said.

By tracking, the intensity of the fluorescent KTRs, the bioengineers could tell whether kinase was active or inactive. Kinases are important regulators of cellular activity. The Stanford technique allows researchers to see how specific levels of kinase activity either promote health or trigger disease inside a living cell.

Covert’s team spent more than a year working on the technique. So far they have successfully applied the KTR approach to five kinases, and they believe that KTR technology could be extended to other kinases, which would make it a widely available and useful tool in drug discovery.

“I imagine you wanted to discover a new drug,” Covert said. “You could throw KTRs into a cell culture and observe kinase activity under different conditions.”

Other Stanford co-authors of the study are postdoctoral scholars Jacob Hughley, Regan Reichert, Kyna Bryan, research associates, and professor of medicine.

The work was supported by the National Institutes of Health, the Human Frontier Science Program and the Paul G. Allen Family Foundation. The Stanford Office of Technology Licensing has filed a provisional patent application based upon the work.

The Department of Bioengineering is administered jointly by the School of Engineering and the School of Medicine.

Markus Covert and his colleagues have developed a technique allowing them to observe and compare kinase activity in healthy versus diseased cells.

Tom Abate is the associate director of communications at Stanford Engineering.
to social interaction,” he said. They can find socializing — even mere eye contact — painful. Outpatient and other methods he and his assistants have invented, they were able to both manipu-
late and monitor activity in specific nerve-cell clusters, and thereby to connect them, in some brains, in real time while the animals were exposed to either murine newcomers or inanimate objects in various lab-
oratory environments. The mice’s behavioral responses were captured by video and compared with simultaneously recorded brain-circuit activity.

In some cases, the researchers observed activity in various brain centers and nerve-fiber tracts connecting them as the mice variously examined or ignored objects. When other experiments involved stimulating or inhibiting impulses within those circuits to see how these manipulations affected the mice’s social behavior.

To avoid confusing simple social interactions with mating- and aggression-related behaviors, the researchers restricted their experiments to female mouse pairs. The mice selected for the research were related to two regions in the brain stem called the ventral tegmental area. The VTA is a key node in the brain’s reward circuitry, which produces sensations of pleasure and can be critical to success in such survival-improving activities as eating, mating or finding a warm shelter in a stressful environment

The VTA transmits signals to other cen-
ters throughout the brain via tracts of nerve fibers, including a chemical called dopamine, at contact points abutting nerve cells in these faraway centers. When dop-
amine lands on receptors on these nerve cells, it can set off signaling activity within them.

Abnormal activity in the VTA has been linked to a range of human diseases, including Parkinson’s and schizophrenia. For example, in Parkinson’s, it is not thought this area is directly affected but that activity in the VTA may be implicated in the disease either directly or through the stimulation of associated tracts.

Deisseroth and his colleagues used mice whose dop-
amine-secreting VTA nerve cells had been engineered to express optogenetic control pro-
teins that could set off or inhibit signaling in the cells in response to light. They observed that enhancing activ-
tivity in these cells increased a mouse’s penchant for social interaction. When a newcomer was introduced into its cage, it came, it saw, it sniffed. Inhibiting the dopami-
nergic VTA cells had the opposite effect: The host lost much of its interest in the guest.

On the other hand, such manipulations of the VTA’s dopaminergic cells had no effect on the mice’s penchant for exploring novel objects (a golf ball, for example) placed in their cages. Nor did it change their overall propensity to move around. The effect appeared to be specific for social interaction.

Finding out exactly which dopaminergic projec-
tions from the VTA, traveling to remote brain structures, were critical for this function generation ex-
ploratory social behavior required designing a new monitoring methodology. The signals traveling along such projection regions were not consistent by background noise, especially when located deep within the brains of ambulatory animals. Deisseroth’s group overcame this by developing a highly sensitive technology capable of picking these tiny signals out of the surrounding noise. The new technique, called fiber photometry, is a sophisticated way of measuring activity in the fibers projecting from nerve cells.

Using a combination of optogenetics and fiber pho-
tometry, the investigators demonstrate that a particular tract projecting from the VTA to a mid-
brain structure called the nucleus accumbens (also strongly implicated in the reward system) was the rel-
evant conduit carrying the impetus for social interac-
tion in the mice. A third technological trick helped determine which recipient nerve cells within the nucleus accumbens were involved in the social-behavior circuitry. That structure’s two types of dopamine receptors are different across species and the cells are differentiated by the types of dopamine receptors, referred to as D1 and D2, on their surfaces. The researchers used experiments in animals bioengineered so that the normally D1-containing cells instead expressed a modified, light-inducible version of that receptor. These experiments, along with complementary experiments block-
ing the D1 receptors with specific drug antagonists, allowed the team to begin to map out how those receptors and their signaling partners were mediating the changes in social behavior. Tripping off those receptors, either by optogenetically inducing in-
hibition or by directly stimulating light-activated forms of these receptors on the target cells, enhanced mice’s social responsiveness.

“Every behavior presumably arises from a pattern of activity in the brain, and every behavioral malfunction arises from malfunctioning circuitry,” said Deisseroth, who is also co-director of Stanford’s Cracking the Neu-
ral Code Program. “The ability, for the first time, to pinpoint a particular nerve-cell projection involved in the social behavior of a living, moving animal will greatly enhance our ability to understand how social be-
havior operates, and how it can go wrong.”

Chairman of the study was shared by gradu-
ate student Logan Grosenick; former graduate stu-
dent Lisa Gunaydin, PhD, (now a postdoctoral fellow at UCSF); former undergraduate Isaac Kauer (now a graduate student at Stanford); and former research assistant Joel Finkelstein (now a graduate student at Princeton). Other Stanford co-authors were professor of psychology and psychiatry and behavioral science Robert Malenka, MD, PhD; graduate student Lien Fenno; postdoctoral scholars Avishhek Adhikari, PhD, and Stephan Lammel, MD, PhD; former postdoctoral fellow Carmen Mirzabekov (now a medical student at UCSF).

Major support for the study came from the Simons Foundation Autism Research Initiative, the National Institute of Mental Health, the National Institute on Drug Abuse, the Gatsby Charitable Foundation, the Wiegars Family Fund and the Stanford Center for Genetics and Genomic Medicine.

Stanford’s Department of Bioengineering, which is jointly operated by the School of Medicine and the School of Engineering, and the Department of Psychiatry and Behavioral Sciences also supported the work.

"Once I saw that — somebody who was at death's doorstep waking up — it was unbelievable," Esquivel said. "I never looked back.

He focused his attention on the babies who weren't being offered liver trans-
plants. Many had a congenital defect in their liver or intestines. In 1995, that team came to Lucile Packard Children’s Hospital in San Francisco. Typically, biliary atresia, which causes liver failure in infancy or toddlerhood, is a key node in the brain's reward circuitry, which produces sensations of pleasure and can be critical to success in such survival-improving activities as eating, mating or finding a warm shelter in a stressful environment.

The next day, she was relieved and happy that he was going to have a new life," Delia said. "He's the whole field was just undergoing a revolution," said Starzl, now professor emeritus at Pennsylvania, whose emunesis in Pittsburgh. Esquivel's scien-
tists restricted their experiments to female mouse pairs.

"There are huge difficulties with transplanting these patients," Esquivel said. Deisseroth pioneered a brain-exploration technique, SAAC K Auv Ar A nd K ArL d ei SS er Oth

Scientists found that stimulating a particular circuit in the brains of mice made them more interested in socializing.

With the patients, transplants were, invari-

ably. So Esquivel began trying to transplant babies. At first, about 70 per-
cent survived.

"Going from 100 percent mortality to 70 percent survival was a huge improve-
ment," Esquivel said. He published his results in 1987 and began advocating that infants and small children should be offered the benefits of transplant.

"I'm instinctively a tremendously good surgeon," said Starzl. "He has the kind of virtuous qualities that you can teach." Those skills allowed Esquivel to consistently rescue the baby’s liver from the blood doesn’t clot, increasing blood loss during surgery. The problem is worse for a small patient who has blood. Hooking up an infant's tiny blood ves-
sels to the donated organ is also difficult. And these children are small for their age because liver failure hampers growth. In short, said Esquivel, "Patients with liver failure are some of the sickest in the hospital.

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ment," Esquivel said. He published his results in 1987 and began advocating that infants and small children should be offered the benefits of transplant.
The first large-scale, comprehensive analysis of the genomic diversity of Mexico — led by researchers at the University of California—San Francisco and the Mexican National Institute of Genomic Medicine — has identified a dazzling mosaic of genotypes and population substructures across the country.

Some groups are as genetically different from one another as Europeans are from East Asians. In particular, the researchers found that variations in Native American ancestry among Mexicans and Mexican Americans significantly affect health outcomes, such as lung function, emphasizing the importance of incorporating fine-scale ethnic information into clinical practice.

The analysis represents an international collaboration of researchers from the United States, Mexico, Spain and the United Kingdom.

"Understanding the genetic structure of a population is important for understanding its population history, as well as designing studies of complex biomedical traits, including disease susceptibility,” said Stanford professor of genetics Carlos Bustamante, PhD. “As we deploy genomics technology in previously understudied populations like those of Latin America, we discover remarkable richness in the genetic diversity of these important groups and why it matters for health and disease."

"Mexico harbors one of the largest amounts of pre-Columbian genetic diversity in the Americas,” said Andre Moreno-Estrada, M.D., PhD, life sciences research associate at Stanford. “For the first time, we’ve mapped this diversity to a very fine geographic scale, and shown that it has a notable physiological impact on an important clinical trait: lung function."

Bustamante, who directs the Stanford Center for Computational, Evolutionary and Human Genomics, shares senior authorship of the study with Esteban de la Rosa, M.D., and Juan Carlos Fernandez Lopez, a researcher at the Mexican genomic institute.

Burchard noted that in lung diseases, such as asthma or emphysema, a person’s ancestry at specific locations on their genes matters. "In this study, we realized that for disease classification it also matters what type of Native American ancestry you have,” he said.

The researchers compared variation in more than 1 million single nucleotide polymorphisms, or SNPs, among 511 people representing 20 indigenous populations of Mexico. They compared these findings with SNP variation among 500 people of mixed Mexican, European and African descent (a category called mestizo) from 10 Mexican states, a region of Guadalajara and Los Angeles, as well as with SNP variation among individuals from 16 European populations and the Yoruba people of West Africa.

The researchers found that Mexico’s indigenous populations diverge genetically along a diagonal northwest-to-southeast axis, with the ancestry becoming more pronounced as the ethnic groups become more geographically distant from one another. In particular, the Seri people along the northern mainland coast of the Gulf of California and a Mayan people known to vary among ethnic groups, like lung function, were the most different.

"This can shape public health and public policy,” Burchard said. “We now have a map of Mexico that will help researchers make those clinical and public health decisions."
Manu Prakash joins other tinkerers at White House for Maker Faire

By Kris Newby

Recently, Manu Prakash, PhD, associate professor of bioengineering, received an invitation to attend the first-ever White House Maker Faire to show attendees how to use a laser-cut music box into a $5 programmable microfluidic chemistry set that can be used to test blood and urine samples.

At the June 18 event, Prakash also demonstrated how to turn a toy microscope out of laser-cut paper, plastic tape and a tiny glass bead.

The 10th annual event, started by Make magazine in 2006, is gatherings where do-it-yourself enthusiasts show off their homemade projects and teach others how to make things using new technologies, such as 3-D printers, laser cutters and desktop machines.

President Barack Obama hosted the first-ever White House Maker Faire to celebrate our "nation of makers" and to help empower America’s students and entrepreneurs to invent the future.

Prakash, who grew up in the mega-city of India with a reflexive interest in technology, is a leader in the frugal-maker movement. At Stanford, he works with students from bioengineering, medicine and Bio-X to re-engineer expensive, complex, health-related devices to make them better, faster and cheaper.

His team also focuses on developing affordable science tools to inspire global innovation. To that end, Prakash recently launched an educational initiative called the 100,000 Microscopes for the Planet project, which build-your-own-microscope kits will be shipped to the first 10,000 people who pledge to share their microscope images and experiments in a free, online microscopy manual.

"I’m so happy that the White House is looking at ways to celebrate scientific curiosity and invention," Prakash said.

Kris Newby is communications manager at Spectrum, the Stanford Center for Clinical and Translational Research.

Stanford to host 10th annual Mood Disorders Education Day

On June 28, Stanford Medicine will host the 10th Annual Mood Disorders Education Day for patients, families, caregivers, friends and others in the community interested in mood disorders.

The program will include discussions of recent treatment advances; the neuroscience of mood disorders; the importance of early intervention; and the role of genetics and optimizing infertility treatments.

The program runs from 9:45 a.m. to 2:30 p.m., with registration starting at 8:30 a.m. The event includes a continental breakfast and lunchtime snacks.

The program is free and open to the public. For registration and more information, please visit www.bipolar.org.

From left, Jane Chen, David Lang and Manu Prakash attended the Maker Faire at the White House on June 18.