INSIDE STANFORD MEDICINE

Volume 8, No. 9 ■ May 9, 2016 ■ Published by the Office of Communication & Public Affairs

A video game allows players to try to design an RNA molecule that could help streamline a new tuberculosis test.

Page 4

Biodesign at 15: New name and new focus

By Ruthann Richter

As a specialist in heart rhythm problems, Uday Kumar, MD, always thought there had to be a better way to monitor the cardiac rhythm activity of his patients when they were outside the clinic, going about their usual activities. Traditionally, patients were prescribed a camera-sized device, hooked to their body via electrodes, to track their heart rate during the day and while sleeping.

These devices have been around for decades, "but they are cumbersome and difficult to use," Kumar said. "I think this is a need that people had overlooked for a while: something you could use to monitor patients with a suspected arrhythmia that is more cost-effective and easier for the patient to use."

As a fellow in the Stanford Biodesign Program in 2005-06, Kumar set his sights on finding a more cost-effective, user-friendly solution. His invention, the ZioPatch, which has been worn by more than 400,000 patients, is one of dozens of innovative devices to emerge from the the program's innovation process, which has become the international model for inventing new medical technologies.

Focus on affordability

This year, the program celebrates its 15th anniversary. It has been renamed the Stanford Byers Center for Biodesign and is moving forward with an emphasis on creating new health technologies that not only benefit patients, but also take into consideration the economic challenges of health care today, said Paul Yock, MD, founder and director of the program at Stanford.

"We have been very successful in training high-tech innovators in the last 15 years," said Yock, a professor of bioengineering and of medicine, who is a successful inventor himself. "Going forward, with the monumental changes in health care and the many cost pressures on the system, we need to create technology that enhances care and does it in a way that's not unduly expensive. That is a sea change."

The center is being renamed in honor of longtime Silicon Valley venture capitalist Brook Byers, who has mentored, coached and supported fellows since the program's inception.

"This program is uniquely positioned to improve human health around the world," Byers said. "Their fellows and medical innovations change health care and have already directly benefited hundreds of thousands of patients. And they're inspiring and empowering others by sharing best practices globally."

Legacy of inventions

Since the program's launch in 2001, it has trained

See BIODESIGN, page 6

NORBERT VON DER GROEBEN

(From left) Biodesign fellows Veronique Peiffer and Richard Timm work with lecturer Ross Venook on ideas for solutions to unmet health-care needs.

At children's hospital, parents mentor parents

By Ruthann Richter

Michele Ashland's daughter was just a month old when Ashland learned in a phone call from her pediatrician that her newborn suffered from a life-threatening liver disease and might need a transplant to survive. She brought her ailing child to Lucile Packard Children's Hospital Stanford, feeling overwhelmed.

GISELLE POTTER

"I landed here knowing nothing about liver disease, transplantation or hospitals," said Ashland, now an employee at the children's hospital. "I just thought the worst. I wondered, 'Am I signing her up for a lifetime of being in the hospital?' You feel so alone."

As it turned out, her daughter would indeed need a liver transplant. With help from the health-care team, Ashland taught herself about liver transplants and learned how to navigate the medical and insurance systems, manage her daughter's rigorous schedule of anti-rejection drugs and keep her safe from marauding pathogens, which can easily defeat transplant patients.

Emotional and practical support

Four years after the 1995 procedure, Karen Wayman, PhD, the developmental specialist on the liver team, recruited Ashland and other parents to give feedback on the transplant process and suggest ways to better support families in caring for their children after transplant. That marked the start of the parent mentor program at the children's hospital, in which experienced parents offer care-management strategies, as well as a shoulder to cry on, to parents of youngsters newly diagnosed with devastating medical conditions.

The program, the first of its kind in the country, now includes 15 trained parent mentors, who are paid for their work and are essential members of the health-care team, said social

See MENTORS, page 7

Promoting abstinence, fidelity for HIV prevention ineffective, study finds

By Ruthann Richter

The U.S. government has invested $1.4 billion in HIV prevention programs that promote sexual abstinence and marital fidelity, but there is no evidence that these programs have been effective at changing sexual behavior and reducing HIV risk, according to a new School of Medicine study.

Since 2004, the U.S. President's Emergency Fund for AIDS Relief, known as PEPFAR, has supported local initiatives that encourage men and women to limit their number of sexual partners and delay their first sexual experience and, in the process, help to reduce the number of teen pregnancies. However, in a study of nearly 500,000 individuals in 22 countries, the researchers could not find any evidence that these initiatives had an impact on changing individual behavior.

Although PEPFAR has been gradually reducing its support for abstinence and fidelity programs, the researchers suggest that the remaining $50 million or so in annual funding for such programs could have greater health benefits if spent on effective HIV prevention methods. Their findings were published online May 2 and in the May issue of *Health Affairs*.

"Overall we were

See ABSTINENCE, page 7

Scientists identify age-dependent changes in pancreatic function

By Krista Conger

Age-related changes in the human pancreas govern how our bodies respond to rising and falling blood sugar levels throughout our lifetimes, and could affect whether we develop diabetes as adults. But it's been nearly impossible to study this process in detail because human pancreatic tissue is not readily available.

Instead, most researchers have relied on animal models to learn more about the development and function of the pancreas.

Now researchers at the School of Medicine have for the first time compared the patterns of gene expression in the insulin-producing cells and other cells of the pancreas from dozens of deceased donors ranging in age from 6 months to 66 years. They found significant differences in gene expression patterns and DNA modifications between donors under the age of 9 and those older than 28.

The findings, published April 28 in *Cell Metabolism*, highlight the importance of two genes not previously implicated directly in pancreatic function, and show that the pancreas continues to develop and mature during the first decades of life. They may also have implications for current clinical trials testing stem-cell-based therapies for diabetes.

STEVE FISCH

Analyzing human pancreatic tissue, rather than relying on animal models, helped Seung Kim and his colleagues better understand how the organ's function changes as we age.

"Studying human islet cells has been a major challenge in the field of diabetes research for decades because the pancreas essentially digests itself shortly after a person's death," said professor of developmental biology Seung Kim, MD, PhD. "We've developed a nationwide network capable of removing and studying pancreatic tissue from organ donors as young as 6 months and as old as 66 within about a day and half after death. This gave us an unprecedented opportunity to chart changes in gene expression spanning the course of a lifetime."

Kim is the senior author of the study. Postdoctoral scholar Efsun Arda, PhD, is the lead author.

'A tour de force'

"This study is a tour de force," said Andrew Stewart, MD, the director of the Diabetes, Obesity and Metabolism Institute at the Mount Sinai School of Medicine who is unconnected with the study. "It is very important to the field of diabetes research."

In the study, Kim, Arda and their colleagues identified two proteins never before directly implicated in pancreatic function whose expression increases as a person ages. Increasing the expression of one of the proteins, SIX3, in the insulin-producing cells isolated from younger donors enhanced their ability to respond efficiently to rising glucose levels.

"Pancreatic islets, which are the sites of insulin production, mature and change in their function after a baby is born," said Kim. "We think our findings suggest that this maturation process goes on for nearly a decade. There's been a growing realization among diabetes researchers that human islet development differs significantly from islet development in typical laboratory animals like mice."

Cells in the pancreatic islets called beta cells are responsible for modulating the body's response to the rise and fall of blood glucose levels after a meal. When glucose levels rise, the beta cells release insulin to cue cells throughout the body to squirrel away the sugar for later use. Type 1 diabetes is caused by a failure to produce insulin; Type 2 diabetes is caused by combined deficits in the body to respond to and make insulin. Both types have been linked to reductions in the number of insulin-producing beta cells.

Although beta cells proliferate robustly during the first decade or so of life, this proliferation slows dramatically with age. Understanding the age-related signals that cause this slowdown could one day lead to new diabetes treatments. But something more significant than the changes in cell number is also going on. Studies in rodents and in human fetal beta cells have showed that the responses of very young beta cells to increases in blood glucose are blunted when compared to their more-mature counterparts.

Sorting the cells

Kim and his colleagues worked for over six years to develop a multi-institutional collaboration to quickly collect pancreatic tissue and isolate and analyze islet cells from newly deceased donors. They also developed a unique cell-sorting technique to isolate islet cells from other cells in the pancreas. Once they had pure populations of cells, they compared their patterns of gene expression, as well as changes in the structure of the DNA.

> "Studying human islet cells has been a major challenge in the field of diabetes research."

"We identified hundreds of genes that are dynamically regulated in islet beta cells during the journey from childhood to adulthood," said Kim. "One gene, SIX3, turns on sometime around age 9. We wondered whether its expression might change the function of the beta cell." Forcing the expression of SIX3 in beta cells obtained from children under the age of 9 improved the ability of the cells to secrete insulin in the presence of glucose, the researchers found.

SIX3 and a related gene, SIX2, with a similar pattern of expression in human beta cells, encode proteins known as transcription factors that control the expression of many other genes in the cell. Although they have not been implicated directly in pancreatic function, genome-wide association studies have linked the presence of a mutation near the genes to an impaired ability to properly manage fasting blood-glucose levels.

"This is a tantalizing link," said Kim. "It appears that genes whose expression changes from childhood to adulthood may be disproportionately associated with an increased risk for diabetes."

Only in humans

Importantly, SIX3 and SIX2 are not expressed in mouse beta cells.

"This is why it is so important to study human tissue," said Kim. "Until now there has been no way of knowing the gradual changes that happen over a period of years."

Kim and his colleagues are planning to continue their studies of pancreatic and islet-cell development as part of a Stanford focus on diabetes and metabolism research. The researchers also anticipate that their gene expression data and newly described islet-cell isolation technique, coupled with the ongoing tissue procurement effort, will be helpful to others studying pancreatic development and diabetes.

"This is a unique and valuable resource for researchers wishing to begin to understand how gene expression is dynamically regulated in human islet cells," said Kim. "Our study charts a new road map for researchers working to use stem cells to replace human islet cells by highlighting changes that normally occur and should perhaps be taken into consideration when analyzing cells for transplant."

The team's work is an example of Stanford Medicine's focus on precision health, the goal of which is to anticipate and prevent disease in the healthy and precisely diagnose and treat disease in the ill.

The study was funded by JDRF, the National Institutes of Health, the Department of Veterans Affairs, the Vanderbilt Diabetes Research and Training Center, the Helmsley Charitable Trust, the H.L. Snyder Foundation, the Elser Foundation, the Doolittle Trust and the Howard Hughes Medical Institute.

The project grew out of the NIH-funded Beta Cell Biology Consortium. Kim and his colleagues are members of a new consortium named the Human Pilot Resource Network that recognizes the importance of studying human tissues.

Other Stanford co-authors of the study are postdoctoral scholars Lingyu Li, PhD, and Heshan Peiris, PhD; former postdoctoral scholar Robert Spitale, PhD; data scientist Jennifer Tsai; former life sciences research assistant Eduardo Torre; life sciences research assistants Yenny Rosli and Jing Wang; research assistant Xueying Gu; senior bioinformatics scientist Kun Qu, PhD; professor of genetics Michael Snyder, PhD; and professor of dermatology Howard Chang, MD, PhD.

Stanford's Department of Developmental Biology also supported the work. **ISM**

Translational Research and Applied Medicine Program symposium set for May 20 in Berg Hall

The Translational Research and Applied Medicine Program will hold its annual research symposium from 9 a.m. to 4 p.m. May 20 in Berg Hall, at Li Ka Shing Center for Learning and Knowledge.

Registration and breakfast begin at 8:30 a.m. The theme this year is precision medicine.

Two speakers from industry — Robert Chess, MBA, chairman of Nektar Therapeutics; and Frederic de Sauvage, MD, PhD, vice president of Genentech — will join several Stanford faculty members to discuss how precision medicine is applied in their areas of expertise.

Presentations will cover a diverse number topics, including hyperinsulinemic hypoglycemia, dengue, pharmacogenomics and cancer therapies.

Six recipients of TRAM pilot grants will also speak about the research their grants supported.

Unique to this year's program will be a performance by the acclaimed St. Lawrence String Quartet, which will present a special musical program called "Precision Listening — with Strings Attached."

The event is free, but attendees are encouraged to consider making a donation to support music at Stanford.

Register to attend the symposium at http://tram2016.eventbrite.com. **ISM**

INSIDE STANFORD MEDICINE

Inside Stanford Medicine is published monthly in July and December and semi-monthly the rest of the year.

is produced by
Office of Communication & Public Affairs
Stanford University
School of Medicine
3172 Porter Drive
Palo Alto, CA 94304
Mail code 5471
(650) 723-6911
http://med.stanford.edu/news/

Paul Costello
Chief communications officer
Susan Ipaktchian
Director of print & Web communications
John Sanford
Editor
Robin Weiss
Graphic designer

Send letters, comments and story ideas to John Sanford at 723-8309 or at jsanford@stanford.edu. Please also contact him to receive an e-mail version of *Inside Stanford Medicine*.

STANFORD MEDICINE

5 QUESTIONS

an occasional feature in which an expert answers five questions on a science or policy topic

Rita Hamad on link between poor areas, diabetes

In the 1980s, as a wave of refugees entered Europe, the Swedish government established an immigration policy that dispersed families to neighborhoods distributed across the country in an almost random fashion. This strict dispersal policy unwittingly created the perfect setup for a natural experiment in which researchers could look for causal relationships between neighborhood quality and population health.

Three decades later, a research team from the Stanford School of Medicine, UC-San Francisco and Lund University, in Sweden, used this natural experiment to look at the effects of neighborhood quality on diabetes risk in a study published April 27 in The Lancet Diabetes & Endocrinology.

In this study, the researchers found that refugees assigned to housing in deprived neighborhoods had a 15 to 30 percent higher chance of developing Type 2 diabetes than counterparts assigned to less-deprived areas. These data were culled from records of 61,386 immigrants, ages 25 to 50, who arrived in Sweden between 1987 and 1991.

Study co-author, Rita Hamad, MD, MS, MPH, an instructor of medicine at Stanford, recently shared her thoughts with writer Kris Newby about this research and how it might be used to help governments assimilate refugees who have recently fled the war-torn country of Syria.

1 How did you determine neighborhood quality from data?

HAMAD: Sweden, like many European countries, collects centralized, real-time data on health-care access, medication prescriptions, income, housing, education and how many people live in each home. We don't have that kind of data access in the United States.

For the Sweden study, we created a composite ranking that factored in levels of poverty, unemployment, average schooling and how many people were enrolled in social welfare programs. Then we categorized neighborhoods as high-deprivation, moderate-deprivation or low-deprivation.

Rita Hamad

2 Why do poor neighborhoods increase diabetes risk?

HAMAD: We're still working on this analysis, but we hypothesize that deprived neighborhoods make it harder for residents to access healthy foods and good health care. There may be fewer opportunities for education and employment, making it harder for them to purchase quality food and health care. And the chronic stress associated with living in a high-poverty or high-crime area might contribute to the onset of diabetes.

3 What was the most surprising finding?

HAMAD: After analyzing 10 to 20 years of health data, we were surprised to find that living in a deprived neighborhood had a cumulative effect on diabetes risk, even when about half of the refugees later moved to a different neighborhood. Their diabetes risk increased by 9 percent on average for every five years after they were settled in high-deprivation areas.

4 Based on these findings, what will you research next?

HAMAD: We want to do this analysis in other settings and countries. Denmark is next, and we will be traveling there in May with funding from Stanford's Center for Population Health Sciences. It's pretty amazing that we will be able to access several decades' worth of health and socioeconomic data on almost all 5.6 million individuals living in Denmark.

Within Sweden we're continuing to work with our collaborators at Lund University. They have a lot of great data on neighborhood characteristics such as walkability and food access. Next, we want to analyze the effect of neighborhood quality on other outcomes like mental health or child health.

5 How might your findings influence policy abroad and in the United States?

HAMAD: Our data suggest that decisions affecting the settlement and integration of immigrants can have long-term consequences for the health of the new arrivals, and that these societies may end up paying the price decades later if refugees don't receive adequate support upfront.

Even though the U.S. doesn't have a national health-care program like Sweden's, the health care of vulnerable populations such as refugees eventually hits everyone's bottom line. People with poor health-care access end up in emergency rooms and on Medicare and Medicaid, and these costs get passed on to taxpayers. Our study suggests that making upfront investments in social services and better neighborhoods for disadvantaged groups can prevent costly chronic diseases such as diabetes. **ISM**

Students delve into medical interests through research projects

By Tracie White

Ulysses Rosas, a fourth-year medical student, was inspired to become a physician by the excellent care he received from his childhood doctors. So it's not surprising that when he went searching for a topic to research during medical school, he chose one focused on bedside care.

"I had a lot of good doctors growing up who encouraged me to do well in school," said Rosas, who saw a physician once per month for orthopedic problems until he was 10. An explanation of his research project was displayed on a poster board May 5 at the 33rd Annual Medical Student Research Symposium at the Li Ka Shing Center for Learning and Knowledge. His project focused on how best to get medical students up to speed in hands-on care as they head off to residency programs, where virtually overnight they become full-fledged doctors.

Rosas was one of about 45 medical-student presenters who displayed the research they had conducted between heavy course loads, clinical rounds and studying for board exams. Each Stanford medical student is required to conduct at least one quarter of research, but most do more than that.

Opportunity to focus on interests

"This is an opportunity for students to take their interests and really focus in on them," said Laurence Baker, PhD, director of the Scholarly Concentration Program, a required program of study for medical students that promotes in-depth learning and scholarship. "This is the first time for many making the transition from student to the role of 'thinker' as a real investigator."

Rosas, who has chosen a career in internal medicine, will be staying at Stanford Medicine after he graduates in June for his residency program. As a soon-to-be resident himself, he was particularly interested in the best way to gain the necessary new skills that may not have been taught in medical school — such as how to read an EKG, or respond to hospital emergency codes.

"How do you tell someone they have cancer? Or what do you do when a patient dies?" said Rosas. Pointing to his poster board, he explained that his research involved measuring the success of a voluntary four-day course to prepare students for their residencies. The results? "Students who did the course increased their level of confidence and reduced levels of anxiety," he said.

NORBERT VON DER GROEBEN

Ulysses Rosas, a fourth-year medical student, discusses his project May 5 at the 33rd Annual Medical Student Research Symposium.

NORBERT VON DER GROEBEN

Angela Guerrero discusses her project, "Retrospective analysis of inpatient dermatology consultations for cancer patients," with Charles Prober, senior associate dean for medical education.

Who's healthier: Americans or Brits

The students' research, which was being judged by faculty and staff, ranged across a variety of topics, including deep dives into primary care, basic science and public health issues.

One project by student Thanh Truong posed the question: Who is healthier, Americans or British people? The Brits won, at least when it comes to rates of diabetes and hypertension.

"It's fun to see the final projects," said Lars Osterberg, MD, associate professor of medicine and one of the judges for the event who made the rounds interviewing students. "That the students manage to do all this on the side, while doing all their other work, it's just amazing."

The symposium drew a crowd of spectators, among them students and faculty members. At the end of the event, the judges picked 10 winners of the poster competition. They received a monetary award funded by the Stanford University Medical Center Alumni Association.

Some of the projects are still in progress. All have a Stanford faculty adviser. Funding comes from a variety of outside fellowship awards and internal fellowships from the Medical Scholars Research Program.

TB in Brazil

Second-year student Tarub Mabud chose to explore his interest in global health by researching the problem of the high transmission rates of tuberculosis among prisoners in Brazil. Incarceration rates in Brazil are some of the highest in the world, the prisons intensely overcrowded, due primarily to the drug trafficking in the region, Mabud said.

The project involved a mathematical modeling of various strategies for controlling the spread of TB. Mabud also spent a summer in Brazil visiting prisons.

"There is a lot of TB in prisons around the world due primarily to overcrowding," Mabud said.

He conducted data analysis comparing the prison populations in Brazil to a national database and found the risk of TB increased dramatically the longer the time of incarceration. The risk of prisoners in Brazil contracting TB was 20 times that of Brazil's general population.

"I've been working on this project for about a year," Mabud said. "I have about two more months. There's always the hope to publish, right?"

Across the room, Sara Aziz, another second-year student, was busy explaining her research project on deep brain stimulation to one of the judges. She described the process of how neuroscientists drill holes into the skull of a patient with Parkinson's disease to implant electrodes on specific parts of the brain. A medical device called a "brain pacemaker," implanted beneath the clavicle, sends electrical impulses to the brain via these electrodes.

"It's very cool how little we know about the brain," Aziz said. "There is so much to learn, and I think that is very exciting." **ISM**

Video game aims to help build a better test for tuberculosis

By Jennie Dusheck

Researchers at the School of Medicine are releasing a new version of a web-based video game that will harness the creative brain power of thousands of nonscientist players.

The goal in coming months is for Eterna Medicine players to design a molecule that could help spur the development of a new tuberculosis test.

Tuberculosis infects a third of the world's population and kills about 1.5 million each year. Yet health organizations lack a simple-to-use blood test that can detect active infection in many patients, especially in remote villages.

Like a previous iteration of the Eterna game, the new version challenges players to build molecules of RNA with increasingly difficult-to-design shapes.

RNA is DNA's inventive cousin. DNA molecules form the standard two-stranded double helices; their threadlike shape is stable and comparatively stiff. In contrast, RNA is single-stranded, floppy and can spontaneously fold into myriad shapes. Each shape has its own biological properties, many of which can be useful to biomedical researchers.

Eterna's co-creator Rhiju Das, PhD, said Eterna Medicine could someday allow citizen-scientists to invent their own pharmaceuticals. "It's going to sound like science fiction," he said. For now, Das, an associate professor of biochemistry at Stanford, is turning loose 100,000 registered Eterna players to pilot a new route to controlling the tuberculosis pandemic.

Games with real-life consequences

Eterna, the first version of the video game, was launched five years ago as a way to let nonscientists design potentially useful biomolecules that are stable enough to function inside a living cell. Over the years, the players have become more and more expert in designing complex RNA molecules. They are so good at it now that the players recently co-authored an article in the *Journal of Molecular Biology* describing a set of rules for predicting how difficult it will be to build a given RNA molecule.

Now Das has set a new challenge in front of them: design a molecule that could help save the lives of millions of people.

Recently, assistant professor of medicine Purvesh Khatri, PhD, and his team came up with a test that can accurately diagnose TB from a simple blood sample. The test looks at the expression levels of three different genes. Cells "express" genes when the cell transcribes a gene into a length of RNA.

In the Khatri lab's TB test, when the three genes are expressed in certain proportions, doctors know the patient has TB. But how to calculate those proportions in a simple test on a stick — like a pregnancy test — is the challenge. To do so, Das said, they need a molecule that can calculate the proportions of three molecules. Right now, there's no single molecule that can make that calculation.

But Das said the Eterna game, powered by the minds of thousands of players, can theoretically create a molecule capable of such a calculation. His hope is to get tens of thousands of designs, of which perhaps a thousand may have potential. Das' lab will then test all of these molecules to see how well they work in the lab. If successful, a subset of 10 to 20 molecules will be tested to see which work best in a real stick-test.

Said Das, "Eterna Medicine is a little different from the original Eterna because we are trying to recruit people to make something with an eventual real-world impact."

Molecular problem-solver

When a person is being tested for tuberculosis with the Khatri TB test, RNA molecules circulating in the blood reveal the levels of expression of three genes. If Eterna players succeed, they'll come up with an Eterna-built RNA molecule, called "OpenTB," that has three parts. RNA readily binds to other RNA molecules. So, if designed right, each part of OpenTB can bind to one of the TB-related RNA molecules. And when each TB-related RNA from patient blood binds to OpenTB, it will change OpenTB's shape.

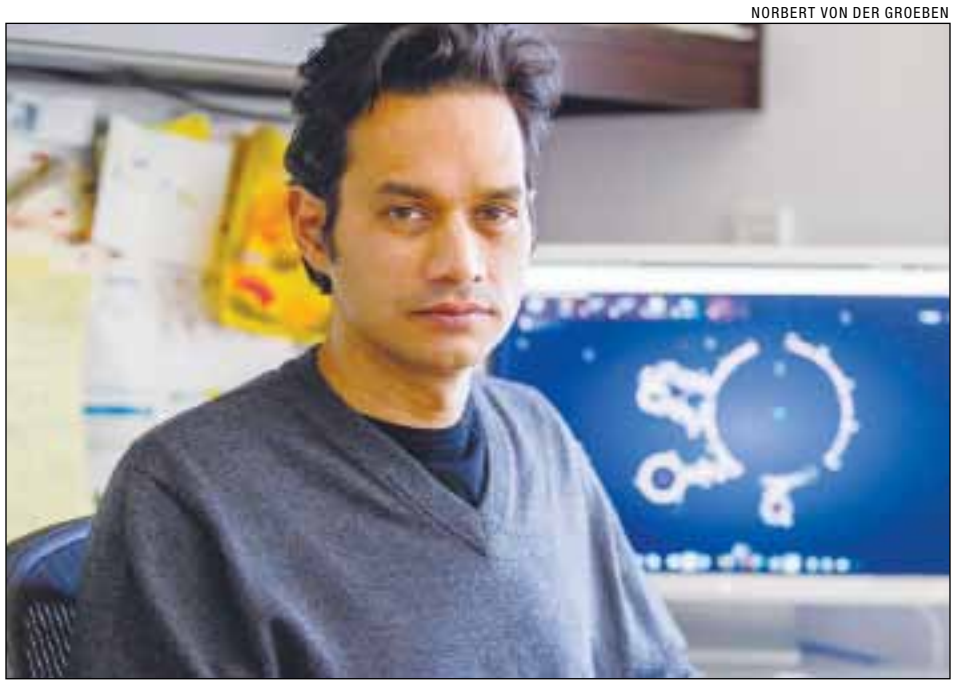
The OpenTB molecule will assume different shapes depending on the proportions of the three kinds of TB-related RNA present in the blood sample. "If I have a lot of RNA molecules A and B around," said Das, "OpenTB will fold into shape 1. But if there's a lot of C around, OpenTB will fold into shape 2."

For Das' plan to work, shape 1 also must be able to bind a fluorescent tag, while shape 2 must not bind the tag. So individual molecules with shape 1 would emit light and those with shape 2 would not.

By measuring the brightness of the light, said Das, you can calculate what

CHARLIE WILKES

NORBERT VON DER GROEBEN



(Top) An Eterna player who goes by the screen name "elves" and postdoctoral scholar Johan Andreasson. (Above) Rhiju Das says a game like Eterna Medicine could someday enable citizen-scientists to invent their own pharmaceuticals.

proportion of Eterna molecules have folded into shape 1, revealing the proportion of RNAs A and B relative to C. If the light is above a certain threshold of brightness, you know the patient has active tuberculosis.

Perfect challenge for Eterna players

Khatri said the idea for using a TB test came about when he and Das were seated together at a conference having dinner. They got to talking, he said, and realized that the TB test might be a perfect challenge for Eterna players. But Das told him that anything more complicated than three or four genes would involve so many possible configurations, it would be almost impossible to solve.

"I love this idea because it changes the biological research paradigm," Khatri said. "If successful, it would allow us to say, 'We can use publically available data — ultimately provided by patients themselves — to find a diagnostic signature of one of the biggest killers of mankind. And then we can engage the public to design molecules that can help deploy that test to help other patients using a video game platform.'" ISM

Trauma team mobilizes to save 10-year-old's hand — and life

By Erin Digitale

When the emergency call came on the evening of Oct. 19, 2015, doctors on Stanford's pediatric trauma team realized the case heading their way could hardly be worse. Ten-year-old Elijah Olivas was being helicoptered from central California to Stanford Medicine's emergency department after being ejected from a moving car during an accident. He had serious head injuries, and his right hand had been severed at the wrist.

The team immediately began planning how to save Elijah's hand — and his life.

"We knew that when Elijah arrived, we'd need to get him to the operating room as quickly as possible but also as safely as possible," said orthopedic surgeon Garet Comer, MD, one of several-dozen experts from the Level-1-certified pediatric trauma service who cared for Elijah.

"Elijah had a potentially life-threatening cranial injury, and we had to ensure that there were no other life-threatening bodily injuries before taking him to the operating room," said pediatric neurosurgeon Samuel Cheshier, MD, PhD. "It was incredibly important because being thrown from a car could have caused a severe bowel or aortic injury, for instance."

While Elijah was en route, the pediatric neurosurgery and trauma teams gathered in the emergency department. Down the hall, the staff of the Ford Family Surgery Center at Lucile Packard Children's Hospital Stanford reserved two operating rooms: one for Elijah's amputated hand and the other for the rest of his body. And a member of the team called Elijah's parents, Jason and Maria Olivas, to reassure them that they would get regular updates on Elijah's condition as they made the four-hour drive from their Santa Maria, California, home. (The couple had not been in the car accident that hurt Elijah; however, their older son, Jason Jr., was in the car and suffered minor injuries.)

As soon as Elijah's helicopter touched down around 10 p.m., his hand was whisked to one operating room at Packard Children's to be washed. While waiting for Elijah to be cleared for surgery, Comer and his orthopedic surgery team identified important structures on the hand to prepare it for reattachment.

Meanwhile, in the emergency department, Cheshier, an assistant professor of neurosurgery at the School of Medicine, got his first look at Elijah's head injury. The skull was fractured in several places. Cerebrospinal fluid was leaking slowly from a tear in the membrane around his brain, and blood was accumulating in the space around his brain. The trauma team used a series of X-rays and CT scans to catalog Elijah's other injuries: facial fractures near his left eye; a broken jaw; several missing teeth; a fracture in his right humerus bone, in the upper arm above where his hand had come off; a few fractured vertebrae; two breaks in his collarbone; and a break in his pelvis. None were critical enough to take precedence over surgery to reattach his hand, which had the best chance of success if it began without delay.

Team effort

"Within a matter of minutes, he had clearance to proceed to the OR," said Comer, a clinical instructor of orthopedic surgery. "It was very impressive how everybody came together."

After Elijah arrived in his operating room, Cheshier placed a pressure monitor in the boy's head to warn the surgeons if the brain hemorrhage began to endanger his brain. If this happened, the neurosurgery team was prepared to perform a craniotomy, in which they would surgically

See TRAUMA, page 5

OBITUARY

Cardiologist and medical innovator Alfred Spivack dies at 87

By Tracie White

Alfred Spivack, MD, a medical innovator who championed the deeper involvement of nurses in patient care, died April 23 at his home at Vi at Palo Alto, a retirement community. He was 87.

He died while swimming in the pool at Vi, but the cause has not been determined, according to his son, Peter Spivack.

A cardiologist and clinical professor emeritus of medicine at the Stanford University School of Medicine, Spivack is remembered for his tenacity in creating change within the world of medicine. He was a "doctor's doctor," his colleagues said, who was always working to improve patient care.

"He loved to challenge what others said was impossible," Peter Spivack said. "In every sense of the word, dad was a teacher. He saw where there was a need and sought to fill it."

Alfred Spivack founded and was the first director of Stanford Hospital's coronary care unit, which opened in 1966. At the time, only a handful of hospitals had CCUs, and many physicians did not yet recognize their value. He founded the hospital's hypertension-anticoagulation clinic and the medical school's popular sports medicine training course.

"When he saw a need to do something, he just did it," said his lifelong friend and colleague Stanley Schrier, MD, professor emeritus of hematology. "When other people might mull about, Al saw an opening, and he just did it."

Spivack also served on Stanford Hospital's board of directors and the medical school's admissions committee, and mentored medical students.

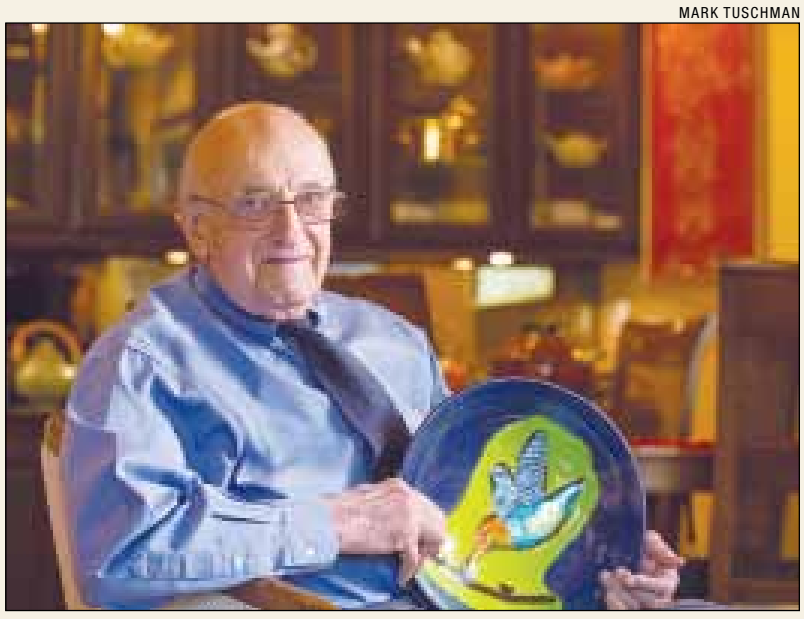
He was among the first to encourage nurses to take a more active role in the care of critically ill cardiac patients, training them in intravenous therapy, electrocardiogram monitoring and defibrillation among other procedures that were primarily restricted to physicians at the time.

'Tireless in making us experts'

"Spivack was tireless in making us experts," said Joan Fair, PhD, one of the coronary care unit's original nurses who is now a cardiovascular researcher. "He really believed we could do these things, and that made us believe we could, too."

Born in Boston in 1928, Spivack graduated from Temple University and Jefferson Medical College. (He received the Alumni Achievement Award from Jefferson University in 2014.) He completed his medical residency in internal medicine at Philadelphia General Hospital and then began a research fellowship in cardiology at Stanford. He remained connected to Stanford until his death, regularly attending the weekly medical grand rounds.

MARK TUSCHMAN



Alfred Spivack, a clinical professor emeritus of medicine who died April 23, also was a ceramicist. He invented a new method of fusing clay and glass.

"Seeing Al sitting front and center every week at medical grand rounds was one of the highlights of my week," said Robert Harrington, MD, the Arthur L. Bloomfield Professor of Medicine and chair of the Department of Medicine. "He always stopped to say hello and talk with me about the history of Stanford. We talked about art and literature, cardiology and diving medicine. Al had a grace and a humility about him that was wonderfully inspiring."

"I'm deeply saddened by this profound loss," said Lloyd Minor, MD, dean of the School of Medicine. "Al was one of the first people I met when I arrived at Stanford. He will be well remembered for his many contributions as an outstanding caregiver, health advocate, and mentor to generations of students and trainees."

Last year, Spivack, along with many of the nurses he helped train, were honored at a dinner celebration of the 50th anniversary of the coronary care unit. He talked about the difficulty of selling the idea of a coronary care unit back in 1966 at what was then the Palo Alto-Stanford Hospital. Some couldn't see the teaching benefit, and others thought the emerging technology of electronic monitoring for heart rhythm, for example, was gimmicky, Spivack said. "They thought it had no viable future," he said.

Today, the role of director of the adult hospital's coronary care unit belongs to Randall Vagelos, MD, professor of medicine at Stanford.

Seeing a need

"Al saw that the future of cardiology was headed toward an environment where patients would be intensely monitored in a high-surveillance nursing unit, where the sickest of patients could still get the best care," Vagelos said. "He understood that all of this was going to depend on nurses. There were clearly not enough doctors to create that kind of surveillance."

"I have a role that he to some degree helped create," he added. "He saw the need, and he just did it."

Spivack had many interests, including scuba diving, underwater photography and collecting and creating art. He was a ceramicist and invented a new method of fusing clay and glass, resulting in works of art that were displayed both on the Stanford campus and abroad. Most recently, he worked as a consultant for Vivus Inc., a drug development company.

He swam regularly with his lifelong friend and colleague Saul Rosenberg, MD, Stanford professor emeritus of hematology. "He and I would swim in the mornings," Rosenberg said. "I was in the pool with him the day before he died. He was an excellent swimmer."

His wife, Anita Spivack, died in 2000. He is survived by his partner, Marjorie Crosby; his son, Peter Spivack; his daughter, Laura Garfinkel; and grandchildren Sarah and Amy Garfinkel and William, Madeleine, Grant and Taylor Spivack. ISM

Trauma

continued from page 4

remove part of his skull to relieve the pressure, while the orthopedic surgeons worked on his hand. Elijah's condition throughout his surgeries was closely monitored by Michael Chen, MD, clinical associate professor of anesthesiology, perioperative and pain medicine, and his team. Because of Elijah's facial fractures, the ophthalmology, otolaryngology and plastic surgery teams consulted on his case in the operating room, too.

By the time the pressure monitor was in place, near midnight, Comer's team had Elijah's hand ready. They brought it from the other operating room to begin the delicate process of reconnecting it to Elijah's arm, fitting together first his bones, then the tendons, then — with the help of a few blood vessel grafts — the veins, nerves and arteries. Finally, after nine hours of surgery, the team closed the skin. They also set Elijah's broken humerus.

Early signs are promising

Early signs for Elijah's hand reattachment looked good: When Comer gently squeezed Elijah's fingernails, he could see the nailbeds blanch and refill, a clue that the reconnected arteries and veins were working.

After that, surgeon Karl Sylvester, MD, medical director of the hospital's pediatric trauma program and associate professor of surgery, performed a bronchoscopy to check on Elijah's airways, and inserted a chest tube to drain fluid from his lungs. Then, still under anesthesia, Elijah was taken to get another CT scan of his brain. The CT showed an expanding hemorrhage, and pressure in his brain was increasing, so Cheshier's neurosurgery team took Elijah back to the operating room for a craniotomy. They evacuated blood, repaired his large skull fracture and fixed the leak of cerebrospinal fluid from his brain.

"Elijah was very fortunate that Stanford has all the technical know-how and physical resources to coordinate a successful response to his life-threatening injuries," Cheshier said. "Not many hospitals can handle this level of trauma in a pediatric patient."

Elijah awakens

When Elijah finally went to his room in the pediatric intensive care unit around 5 p.m. on Oct. 20, the medical team reassured Jason and Maria that their son's surgeries had gone as well as anyone could have hoped. "They also gave us updates along the way, which was awesome," Jason said. Still, he and Maria were worried and fatigued, having stayed up ever since they arrived at Packard Children's at 3:45 a.m. It wasn't until Elijah was brought out of his medically induced coma a few days later that his parents said they breathed a true sigh of relief.

"Elijah woke up yelling, 'What happened? Why am I in the hospital?'" Jason said. "It was a good sign for us." Feeling around in his mouth, Elijah demanded to know why the Tooth Fairy was falling down on the job. "He said, 'I wanna get paid, I'm missing some teeth! Somebody owes me some money!'" said Jason, remembering his joy at this evidence that his son was still himself.

JASON OLIVAS

Elijah Olivas, who suffered a severed hand and other major injuries in a car accident, was treated at Lucile Packard Children's Hospital Stanford.

Elijah stayed at Packard Children's until Nov.16, turning 11 along the way, then moved to a rehabilitation center in Los Angeles to get more help with regaining function in his hand. He finally went home to Santa Maria on Jan. 22. He's now being home-schooled, working to rehabilitate his hand — which has regained some movement — and adjusting to the long-term effects of the accident, including hearing loss from nerve damage. Comer is monitoring Elijah's progress in cooperation with his hometown occupational therapists.

The Olivas family said they will always be grateful for both the lifesaving medical care and the empathy they experienced during Elijah's stay at Packard Children's.

"If we were taking a walk on the floor or eating in the cafeteria and we saw a member of Elijah's care team, they'd always remember us and say, 'Hey, Mr. and Mrs. Olivas, this is what's going on,'" Jason said. "They gave us regular updates every time we saw them, even if we weren't at Elijah's bedside. Everybody really cared — we could tell. We are so thankful." ISM

Biodesign

continued from page 1

more than 1,000 graduate students and nearly 200 fellows. The trainees have founded more than 40 companies and created products used by well over a half-million patients, said Yock, who is also the Martha Meier Weiland Professor in the School of Medicine. These include devices to forestall night terrors in children, prevent infections after surgery, relieve symptoms from an enlarged prostate, provide respiratory support in low-resource settings, as well as to treat dry eyes and women's incontinence.

"Biodesign is a program that exemplifies the concept of precision health. Working at the intersection of medicine, engineering and business, Biodesign fellows are delivering path-breaking solutions to the most pressing human health problems," said Lloyd Minor, MD, dean of the School of Medicine. "Moreover, these innovative fellows go back out into the world, taking with them not just their first invention but their capacity *to keep inventing* — and to teach others how to invent — whether in their own startups, in existing companies or as faculty members in top universities. This is the multiplier effect: We seed the world with people who approach innovation using this proven, needs-based process."

"Over the last 15 years, Stanford Biodesign has had an extraordinary impact on the world," said Persis Drell, PhD, dean of the Stanford School of Engineering. "It has done so in large part because its leadership recognized early on that solving big, complex problems requires teams of scholars from multiple backgrounds and disciplines to work together. Stanford engineers are very proud to be a part of this highly successful collaboration and look forward to continuing to do so."

The program had its genesis in the late 1990s when Bio-X, the university's interdisciplinary biosciences institute, was taking shape. Yock was among a dozen faculty in medicine and engineering with an interest in medical technology innovation who wanted to create a unit within Bio-X, he said. The group was committed to having a fellowship training component in the program and reached out to Josh Makower, MD, MBA, a successful medical technology entrepreneur who had developed an interdisciplinary training initiative while at Pfizer. With help from faculty and industry colleagues, Makower developed the Stanford training approach and became the program co-founder and its first fellowship director.

The new program moved from its temporary headquarters in the Center for Clinical Sciences Research into the James H. Clark Center, the Bio-X hub. Initial funding was provided by a combination of private donors and industry gifts, followed by foundation and grant support, and the program continues to rely on these funding sources today.

In 2003, Tom Krummel, MD, then chair of surgery and a robotics expert, became co-director of the program and actively began recruiting surgeons as fellows. Currently, surgeons will often spend two years, rather than one year, at Biodesign because the second year is when most surgical inventions take on a life beyond the theoretical, Krummel said. "By the second year, the fellows are much closer to having not just a technology but the ability to build a sustainable business," he said.

Paul Yock

Identifying unmet needs

The program selects 12 fellows each year from an international pool of candidates and divides them into teams of four — typically two physicians and two engineers.

For all the fellows, the training process begins with the critically important step of identifying an unmet clinical need, said Makower, a consulting professor of medicine at Stanford. He believes many companies fail at innovation because they start first with a technology and then try to find a place where it might be put to clinical use. But technology will only make meaningful, lasting improvements in how health care is delivered if it addresses a clear need, he said.

To identify compelling needs, the fellows spend two months observing patient care at Stanford's hospitals and clinics, soaking up the clinical experience. As the first fellowship director, Makower said he encouraged fellows to sleep in the residents' on-call room so they could observe every step of the clinical interaction and even visit patients' homes when possible and appropriate to see how they were adhering — or not adhering — to a particular therapy.

During this time, the fellows may identify as many as 200 needs. Then they have to select the two or three that seem most promising, and ultimately choose just one of them.

In the past, Yock said, cost wasn't a primary consideration, but that has changed as a result of increasing pressure from government and private payers.

"We never paid much attention to how much our inventions would cost — or cost the system," he said. "Now we teach the fellows that it's essential to take economics into consideration before, during and after they invent. That's true for the United States' health-care system and in the global health-care environment, where affordability is an even more important factor."

'Objectively take a hard look'

At this stage, too, the fellows have to take into account many other issues that could influence whether a device is successful.

"You have to ask, 'Is there a clear regulatory path?'" said Kumar, now the program's director of strategy and a consulting associate professor of bioengineering. "What is your pathway to reimbursement and is it feasible? Can you protect the intellectual property? What business model will provide sustainability? Is there global play beyond the U.S.?

"Most needs and solutions don't hit all of those," he added. "The challenge is not to fall in love with any one idea but objectively take a hard look and find the one that has the best chance of reaching patients once you take all of these factors into account."

Once fellows have settled on an idea, they begin the process of implementing their solution, possibly developing a prototype and building a plan to help bring it to the marketplace.

To help the fellows better understand the universe of medical technology, the program brings in experts from various fields, including regulatory and patent experts, venture capitalists and marketing specialists, who donate their teaching time, Makower said.

Drawing on these outside advisers "has really crystallized the whole community around the program," he said.

Stanford faculty also teach in the program, which offers one- and two-semester classes for graduate students in medicine and engineering, as well as a courses for undergraduates.

Interest from abroad

Over the years, the program has attracted considerable interest from abroad, leading to collaborations in India, Ireland and Singapore. More recently, Stanford Biodesign helped initiate a program in Japan, which was announced last year by Prime Minister Abe on his visit to the Stanford campus. Innovators trained in these international programs are developing life-changing solutions tailored to the specific needs of patients in their communities.

Through these partnerships, particularly in India and Southeast Asia, "we are trying to absorb their culture of cost-effective innovation," Yock said, and benefit from the experience of entrepreneurs who may live and work in a resource-limited environment. He and his colleagues maintain ongoing relationships with program alumni abroad as they invent and develop technologies and build biodesign training programs in their home countries.

"We are moving the entire fellowship to a more global orientation and will be accepting fellows from any country on a 'best athlete' basis," Yock described. He said the program will expose future fellows to global markets during their training through lectures and visiting speakers, and help make connections for those who want to go to the developing world after their fellowship year.

Yock and his colleagues also have documented the discipline of the biodesign innovation process in a textbook, a 2-inch thick resource that he edited with Makower; Stefanos Zenios, PhD, a professor of business at Stanford; and a team of others. The textbook is being used as a teaching tool in scores of major universities around the world, helping cement the center's role as a global leader. Yock also helped launch the Biomedical Innovation Engineering, Design and Entrepreneurship Alliance, a group of faculty at 100-plus universities who share experiences, challenges and opportunities to advance training in biomedical engineering and innovation.

Makower said the business of developing new medical technology is a tough one, as there may be hundreds of failures for every success. And the profits are modest compared to an internet or social networking megahit, he said. But the payoff in human terms is enormous.

"When you invent a device that addresses a compelling medical need and someone is successfully treated," he said, "there's nothing better than that." ISM

PHOTOS BY NORBERT VON DER GROEBEN

(Clockwise from top left) The Stanford Biodesign textbook is used by health technology training programs around the world. Fellows Craig Stauffer and Richard Timm; James Wall, assistant director of the innovation fellowship program; and fellow Veronique Peiffer discuss a project. Uday Kumar, director of strategy, and Lyn Denend, director of academic programs, discuss the mission of the Stanford Byers Center for Biodesign.

Mentors

continued from page 1

worker Lindsey Martins, who oversees the program.

The mentors, some of whom are fluent in Spanish, offer emotional and practical support to parents of children with cancer, heart disease, cystic fibrosis, diabetes, gastrointestinal disorders and other complex medical conditions, as well as those with infants in the neonatal intensive care unit. In addition to face-to-face interactions with families, the mentors helped develop guides, available in print or online, with tips on relevant issues, such as managing insurance and organizing a child's treatment and medication schedule.

'They relax and let down their guard'

"I used to think of the program as icing on the cake, but now I think it's not just icing — something extra — because how you manage things as a parent can really make a difference in your child's life," said Ashland, whose daughter is now a thriving college junior.

"When I approach families, I tell them I'm a parent and that they can talk to me," said parent mentor Teresa Jurado, whose 26-year-old son has cerebral palsy. "You see their whole face change. It seems like they relax and let down their guard. They don't have to pretend they have it all together."

Angelica Marin, a mother of three from Lathrop, California, said she was struggling to take care of her daughter, 7-year-old Valeria, who was born with a disability that restricts her ability to walk, speak and feed herself. Ashland and Jurado both helped her with the process of securing a wheelchair, set up appointments with the child's dozen or so specialists and arranged for a Spanish interpreter at a time when Marin was still learning English.

"I don't have words to explain just how much they have helped me," she said. "You feel so lost and are afraid of everything. I learned that I'm not alone.

"One piece of advice I always remember is they told me, 'Never give up. There is always a door open for you.'" ISM

Abstinence

continued from page 1

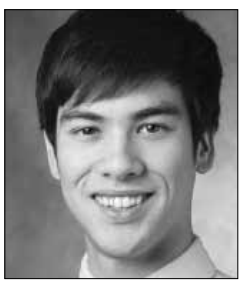
not able to detect any population-level benefit from this program," said Nathan Lo, a Stanford MD/PhD student and lead author of the study. "We did not detect any effect of PEPFAR funding on the number of sexual partners or upon the age of sexual intercourse. And we did not detect any effect on the proportion of teen pregnancy.

"We believe funding should be considered for programs that have a stronger evidence basis," he added.

A human cost

Senior author Eran Bendavid, MD, said the ineffective use of these funds has a human cost because it diverts money away from other valuable, risk-reduction efforts, such as male circumcision and methods to prevent transmission from mothers to their children.

Eran Bendavid



Nathan Lo

"Spending money and having no effect is a pretty costly thing because the money could be used elsewhere to save lives," said Bendavid, an assistant professor of medicine at Stanford.

PEPFAR was launched in 2004 by President George W. Bush with a five-year, $15 billion investment in global AIDS treatment and prevention in 15 countries. The program has had some demonstrated success: A 2012 study by Bendavid showed that it had reduced mortality rates and saved 740,000 lives in nine of the targeted countries between 2004 and 2008.

However, the program's initial requirement that one-third of the prevention funds be dedicated to abstinence and "be faithful" programs has been highly controversial. Critics questioned whether this approach could work and argued that focusing only on these methods would deprive people of information on other potentially lifesaving options, such as condom use, male circumcision and ways to prevent mother-to-child transmission, and divert resources from these and other proven prevention measures.

Abstinence, faithfulness funding continues

In 2008, the one-third requirement was eliminated, but U.S. funds continued to flow to abstinence and "be faithful" programs, albeit at lower levels. In 2008, $260 million was committed to these programs, but by 2013 that figure had fallen to $45 million.

Although PEPFAR continues to fund abstinence and faithfulness programs as part of its broader behavior-based prevention efforts, there is no routine evaluation of the success of these programs. "We hope our work will emphasize the difficulty in changing sexual behavior and the need to measure the impact of these programs if they are going to continue to be funded," Lo said.

While many in the medical community were critical of the abstinence-fidelity component, no one had ever analyzed its real-world impact, Lo said. When he presented the results of the study in February at the Conference on Retroviruses and Opportunistic Infection, he received rousing applause from the scientists in the audience, some of whom came to the microphone to congratulate him on the work.

To measure the program's effectiveness, Lo and his colleagues used data from the Demographic and Health Surveys, a detailed database with individual and household statistics related to population, health, HIV and nutrition. The scientists reviewed the records of nearly 500,000 men and women in 14 of the PEPFAR-targeted countries in sub-Saharan Africa that received funds for abstinence-fidelity programs and eight non-PEPFAR nations in the region. They compared changes in risk behaviors between individuals who were living in countries with U.S.-funded programs and those who were not.

The scientists included data from 1998 through 2013 so they could measure changes before and after the program began. They also controlled for country differences, including gross domestic product, HIV prevalence and contraceptive prevalence, and for individuals' ages, education, whether they lived in an urban or rural environment, and wealth. All of the individuals in the study were younger than 30.

Number of sexual partners

In one measure, the scientists looked at the number of sexual partners reported by individuals in the previous year. Among the 345,000 women studied, they found essentially no difference in the number of sexual partners among those living in PEPFAR-supported countries compared with those living in areas not reached by PEPFAR programs. The same was true for the more than 132,000 men in the study.

The researchers also looked at the age of first sexual intercourse among 178,000 women and more than 71,000 men. Among women, they found a slightly later age of intercourse among women living in PEPFAR countries versus those in non-PEPFAR countries, but the difference was slight — fewer than four months — and not statistically significant. Again, no difference was found among the men.

Finally, they examined teenage pregnancy rates among a total of 27,000 women in both PEPFAR-funded and non-funded countries and found no difference in rates between the two.

Bendavid noted that, in any setting, it is difficult to change sexual behavior. For instance, a 2012 federal Centers for Disease Control analysis of U.S.-based abstinence programs found they had little impact in altering high-risk sexual practices in this country.

"Changing sexual behavior is not an easy thing," Bendavid said. "These are very personal decisions. When individuals make decisions about sex, they are not typically thinking about the billboard they may have seen or the guy who came by the village and said they should wait until marriage. Behavioral change is much more complicated than that."

Level of education

The one factor that the researchers found to be clearly related to sexual behavior, particularly in women, was education level. Women with at least a primary school education had much lower rates of high-risk sexual behavior than those with no formal education, they found.

"One would expect that women who are educated have more agency and the means to know what behaviors are high-risk," Bendavid said. "We found a pretty strong association."

The researchers concluded that the "study contributes to the growing body of evidence that abstinence and faithfulness campaigns may not reduce high-risk sexual behaviors and supports the importance of investing in alternative evidence-based programs for HIV prevention in the developing world."

The authors noted that PEPFAR representatives have been open to discussing these findings and the implications for funding decisions regarding HIV prevention programs.

Stanford medical student Anita Lowe was also a co-author of the study.

The study was funded by the Doris Duke Charitable Foundation and Stanford's Center on the Demography and Economics of Health and Aging.

Stanford's Department of Medicine also supported the work. ISM

Big Data in Biomedicine Conference set for May 25-26 on campus

The 2016 Big Data in Biomedicine Conference, set for May 25-26 at the Stanford University School of Medicine, will focus on advancing precision health by harnessing data from electronic health records, biomedical databases and wearable sensors.

"We are once again thrilled to welcome experts from around the world to our annual Big Data in Biomedicine Conference, where we will continue to work together to advance our vision for precision health — through which we are using big data to anticipate and prevent disease in the healthy and precisely diagnose and treat disease in the ill," said Lloyd Minor, MD, dean of the School of Medicine, who will give introductory remarks at the conference.

The two-day event is expected to draw hundreds of researchers and leaders from academia, health care, government and industry. More than 40 presenters will discuss ways to deploy data analysis and technology in a range of fields, including genomics, cancer, pharmacovigilance, population health, biobanks, microbiota, statistics, machine learning, digital health, and learning health systems.

The annual conference debuted in 2013, thanks to a grant from the Li Ka Shing Foundation. Last year's event brought nearly 500 attendees to the campus, while another 3,000 watched online via live-streamed video.

Among this year's speakers will be Kathy Hudson, PhD, deputy director for science, outreach and policy at the National Institutes of Health; Robert Califf, MD, commissioner of the U.S. Food and Drug Administration; Blake Byers, PhD, general partner at Google Ventures; Shahar Shpigelman, big data analytics manager at Intel; Carlos Bustamante, PhD, professor and chair of biomedical data science and professor of genetics at Stanford; Jody Heymann, MD, PhD, dean of the Fielding School of Public Health at UCLA; and Steve Lohr, a *New York Times* reporter and author of *Data-ism: The Revolution Transforming Decision Making, Consumer Behavior, and Almost Everything Else*.

The 2016 conference is part of Stanford Medicine's Biomedical Data Science Initiative, which strives to make powerful transformations in human health and scientific discovery by fostering innovative collaborations among medical researchers, computer scientists, statisticians and physicians.

To learn more and to register for the conference, please visit http://bigdata.stanford.edu. ISM

JUERGEN FAELCHLE / SHUTTERSTOCK.COM

PHOTOS BY NORBERT VON DER GROEBEN

A taste of medical school

Med School 101, a Stanford Medicine event that offers local teens a glimpse into the world of medical school, was held April 29 at the Li Ka Shing Center for Learning and Knowledge. More than 125 students from six Bay Area schools attended a day of talks and demonstrations. In the "Paging Dr. Gadget" session (above), a student presents his team's suggestion for an invention that would be more hygienic than tissues for dealing with a runny nose. The team came up with iSteam, a device that would first inject steam into the sinuses and then vacuum out the mucus and liquid. A student (top right) peers through a Foldscope, an inexpensive microscope made of folded paper and a bead of glass, in the "Frugal science" session. Students (bottom right) in "The brain whisperer" session learn how electrodes can be used to find out what parts of a living human brain are doing.

OF NOTE

reports on significant honors and awards for faculty, staff and students

Michael Angelo

Ben Barres

Rebecca Bernert

Brendan Carvalho

Mark Davis

MICHAEL ANGELO, MD, PhD, was appointed assistant professor of pathology, effective Nov. 1. His research applies multiplexed ion-beam imaging, which visualizes proteins, to a variety of fields including the evaluation of cancer lesions and the status of immune-cell populations in solid tissues.

BEN BARRES, MD, PhD, professor and chair of neurobiology and professor of developmental biology and of neurology and neurological sciences, will receive the $25,000 Gill Distinguished Scientist Award from the Linda and Jack Gill Center for Biomolecular Science at Indiana University. He will present a lecture on reactive astrocytes at a ceremony in September. His research focuses on glial cells.

REBECCA BERNERT, PhD, was appointed assistant professor of psychiatry and behavioral sciences, effective Oct. 1. She specializes in suicidology and directs the Stanford Suicide Prevention Research Laboratory. Her work investigates therapeutic targets for suicide prevention at all ages and the relationship between sleep and mental health.

BRENDAN CARVALHO, MD, was promoted to professor of anesthesiology, perioperative and pain medicine, effective Dec. 1. He is the chief of obstetric anesthesia. His research focuses on improving the management of post-cesarean and labor pain and on developing pharmacokinetic/pharmacodynamic models of drugs used in pregnancy.

MARK DAVIS, PhD, the Burt and Marion Avery Family Professor and a professor of microbiology and immunology, was elected a foreign member of the Royal Society of London, the oldest extant scientific society, which was established in 1660. He directs the Stanford Institute for Immunity, Transplantation and Infection and is a Howard Hughes Medical Institute investigator. His research focuses on how immune cells recognize antigens.

SARAH DONALDSON, MD, the Catharine and Howard Avery Professor and a professor of radiation oncology, will receive the first annual Women Who Conquer Cancer Mentorship Award, from the Conquer Cancer Foundation of the American Society of Clinical Oncology, in June. She is being honored for her commitment to mentoring young female oncologists. Her research focuses on improving the quality of treatment for children with cancer.

TINA HERNANDEZ-BOUSSARD, PhD, was appointed associate professor (research) of surgery and of medicine, effective Nov. 1. She directs the Surgical Health Services Research Unit at Stanford. Her research uses clinical data sets to evaluate the quality of health-care delivery and for comparative effectiveness research.

SEUNG KIM, MD, PhD, professor of developmental biology, has been awarded a $500,000 grant through the Type 1 Diabetes Program of the Leona M. and Harry B. Helmsley Charitable Trust. Working with other investigators at Stanford and at Vanderbilt University, he will test a new method that aims to use immune cells to enhance the survival of beta cells, which produce insulin.

JONATHAN MALTZMAN, MD, PhD, was appointed associate professor of medicine, effective Nov. 1. He was also appointed staff physician at the Veterans Affairs Palo Alto Health Care System. His research focuses on immunological memory and regulation and their role in organ transplantation.

RAVINDRA MAJETI, MD, PhD, has been promoted to associate professor of medicine, effective Nov. 1. His work focuses on the characterization and therapeutic targeting of leukemia stem cells in human hematologic malignancies, particularly acute myeloid leukemia.

EDWARD MARIANO, MD, was promoted to professor of anesthesiology, perioperative and pain medicine, effective Dec. 1. He is the chief of the anesthesiology and perioperative care service and associate chief of staff for inpatient surgical services at the VA Palo Alto Health Care System. His research focuses on the development of techniques and strategies to improve postoperative pain control and other surgical outcomes.

Sarah Donaldson

ROBERT NEGRIN, MD, professor of medicine, was named the editor-in-chief of a new online journal, *Blood Advances*. It will supplement *Blood*, the American Society of Hematology's existing hematology journal. Negrin's research focuses on immune cells that are involved in responses to cancer or transplants.

KIM ROBERTS, MHA, chief strategy officer and chief administrative officer of physician practices for Stanford Children's Health and chief executive officer of the Packard Children's Health Alliance, was named a *Silicon Valley Business Journal* Power Executive for 2016. The executives were selected by the paper's editorial staff based on reader nominations.

NIGAM SHAH, MBBS, PhD, was promoted to associate professor of medicine, effective Nov. 1. His research uses longitudinal electronic health record data to answer clinical questions, generate insights and build predictive models.

BARBARA SOURKES, PhD, professor of pediatrics and the John A. Kriewell and Elizabeth A. Haehl Director of Pediatric Palliative Care at Lucile Packard Children's Hospital Stanford, received the Compassion in Action 2016 Award from Hospice of the Valley, a San Jose-based organization, in March. She was honored for her service and pioneering leadership in the field of pediatric palliative care.

JOANNA WYSOCKA, PhD, was promoted to professor of chemical and systems biology and of developmental biology, effective Oct. 1. Her research focuses on the genetic regulatory mechanisms underlying cellular plasticity, differentiation, human development and evolution. **ISM**

Tina Hernandez-Boussard

Seung Kim

Jonathan Maltzman

Ravindra Majeti

Edward Mariano

Robert Negrin

Kim Roberts

Nigam Shah

Barbara Sourkes

Joanna Wysocka