INSIDE STANFORD MEDICINE

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The Biomedical Innovation Building will house multidisciplinary teams of engineers, basic scientists and physician-researchers.

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Dean: Physician burnout 'a systemic issue'

By Mandy Erickson

Physician burnout is worsening, but organizations and individuals can counter the trend, speakers asserted at a Stanford Medicine-sponsored conference on the topic.

"This is not just individuals acting out," said Lloyd Minor, MD, dean of the School of Medicine. "This is a systemic issue that we face in the profession."

The American Conference on Physician Health, which took place Oct. 12-13 in San Francisco, attracted 425 attendees, mostly physicians, from 44 states and seven countries. It featured a range of speakers, from medical students to experts on physician burnout. They shared personal experiences, presented research and offered tips on coping with stress.

Tait Shanafelt, MD, the chief wellness officer at Stanford Medicine, noted that nearly half of physicians — 45 percent — currently show at least one symptom of burnout. Not only do burned-out physicians provide lower-quality care, he noted, but replacing physicians who leave because of burnout costs the United States $5 billion a year.

PAUL SAKUMA

The closing panel at the American Conference on Physician Health featured (from left) Andrea Sikon of the Cleveland Clinic; Lloyd Minor, dean of the Stanford School of Medicine; Sara Krevans, president and CEO of Sutter Health; Steve Strongwater, president and CEO of Atrius Health; and Tina Shah, White House fellow of the U.S. Department of Veteran Affairs.

He added that the problem can spiral within an organization: "There's an infectious component of burnout," he said. Other members of the care team "learn cynicism."

Conference speakers agreed that administrative requirements — such as entering information into electronic health records, or EHRs, and filling prescriptions — contribute to physician unhappiness. But they also blamed a toxic culture in many health care organizations, along with a tendency among physicians to deny their own suffering.

'Fear of showing weakness'

Abraham Verghese, MD, professor of medicine at Stanford and an award-winning author, discussed one of the most pernicious effects of physician unhappiness: suicide. When he asked conference attendees if they knew fellow physicians who had killed themselves, nearly all raised their hands. "Every year it takes three medical school classes to replace the physicians who committed suicide," he said.

Verghese related the story of his friend David Smith, the subject of his book *The Tennis Partner*, who struggled with addiction before shooting himself. He said that the "loneliness of doctors" enabled Smith's addiction. "We rarely expose our emotions," he said. "There's a fear of showing weakness."

Conference speakers addressed three avenues to improve physicians' job satisfaction: personal resilience, organizational culture and more efficient processes.

Kelly McGonigal, PhD, a health psychology lecturer at Stanford, encouraged conference attendees to practice "self-compassion." See BURNOUT, page 6

Tissue-specific gene expression uncovered and linked to disease

By Krista Conger

The sequencing of the complete human genome in 2001 was a remarkable achievement. For the first time, researchers could pore over a consensus sequence of an average human, describing many of the genes that make us tick. Differences from this consensus are thought to contribute to the pantheon of human variation that makes each of us uniquely See GTEX, page 6

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Researchers discover particular mutation supercharges tumor-suppressor protein

Cancer researchers have long hailed p53, a tumor-suppressor protein, for its ability to keep unruly cells from forming tumors. But for such a highly studied protein, p53 has hidden its tactics well.

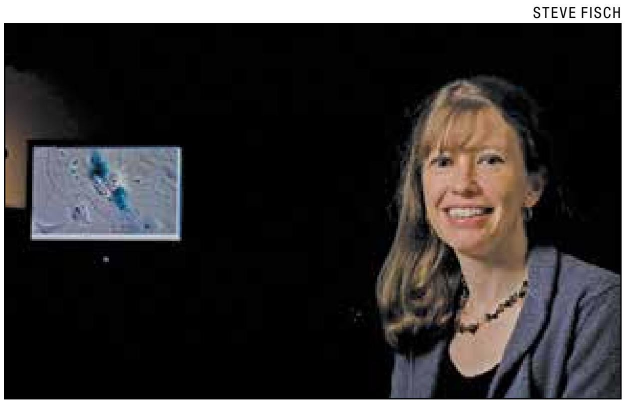
Now, researchers at School of Medicine have tapped into what makes p53 tick, delineating a clear pathway that shows how the protein mediates anti-tumor activity in pancreatic cancer. The team's research also revealed something unexpected: A particular mutation in the p53 gene amplified the protein's tumor-fighting capabilities, creating a "super tumor suppressor."

The protein functions a bit like a puppet master in the genome, guiding the activation or suppression of many cancer-relevant genes in the body. "But if you simply ask how cells with and without p53 are different, you'll see that there are at least 1,000 genes whose expression is affected by p53 status," said Laura Attardi, PhD, professor of radiation oncology and of genetics. "So, getting to the bottom of which of those many genes are critical to tumor suppression is not a trivial question."

Mutated for the better

A paper describing the work was published online Oct. 9 in *Cancer Cell*. Attardi is the senior author. Research associate Stephano Mello, PhD, is the lead author.

STEVE FISCH



Laura Attardi and her colleagues have found a mutation in the p53 tumor-suppressor protein that turns it into a "super" suppressor.

Attardi began sorting out the puzzle by testing the effect of several individual p53 mutations in mice that were predisposed to pancreatic cancer. Any change in p53 activity typically points to trouble: Too little leaves the body susceptible to tumor growth, whereas too much can cause problems in development. But surprisingly, one of the p53 mutants actually kept the mice tumor-free longer, suggesting it was a super version of p53.

"What's incredible about this mutant is that it hit a sweet spot," Attardi said. "Em- See MUTATION, page 7

Newborns with trisomy 13 or 18 can benefit from heart surgery

By Aylin Woodward

Heart surgery significantly decreases in-hospital mortality among infants with either of two genetic disorders that cause severe physical and intellectual disabilities, according to a new study by a researcher at the School of Medicine and his colleagues at the University of Arkansas for Medical Sciences.

Trisomy 13 and 18, which result from having extra chromosomes, often cause heart defects. Infants with the conditions generally die within their first year. Many die within weeks, if not days, of being born.

Thomas Collins

Due to these infants' short life expectancies, their heart conditions are often treated with standard medical care — blood pressure medication, ventilators and intravenous fluids — but not surgery. Many hospitals rarely give parents the option of surgery for their child. "The thought has been that it doesn't make sense to undertake a major heart surgery if the patient's death within a few months is a near certainty," said Thomas Collins, MD, clinical associate professor of pediatric cardiology at Stanford.

But Collins and his co-authors at Arkansas analyzed the outcomes of the 100 babies with trisomy 13 or 18 in the study who had received heart surgery, and recorded the health impacts. What they found was that patients who underwent heart surgery had a significant decrease in mortality, and that the impact lasted for the next two years. "We thought we'd show no difference in survival, but it turns out there's a marked one," Collins said.

Largest study of its kind

A study describing the team's findings was published online Oct. 18 in *Pediatrics.* Collins, the senior author, was on the faculty of the University of Arkansas for Medical Sciences when much of the work was done. The lead author is Katherine Kosiv, MD, a cardiology fellow at the university.

Using data gathered from 44 children's hospitals across the United States between 2004 and 2015, the researchers reported outcomes for nearly 1,600 patients, the largest study ever of infants with trisomy 13, also known as Patau syndrome, or trisomy 18, also known as Edwards syndrome, Collins said.

The researchers found that heart surgery increased survival and hospital discharge on average from 33 percent to approximately 67 percent for these patients, and that this benefit lasted through two years of follow-up. "When we analyzed the survival curves, the data spoke for themselves," Collins said. "Especially for trisomy 18, the number of babies that survive more than doubles after surgery."

Most infants in the study were admitted at less than a day old, and 51 percent of infants in the study who had congenital heart defects died in the hospital or were discharged to hospice. The researchers also found that in-hospital mortality decreased in infants who were older at their admission date, heavier and female, corroborating previous findings.

Challenging the narrative

Collins said his goal is to challenge the narrative surrounding these two conditions, much like how the story of trisomy 21, or Down syndrome, has changed in the last 40 years. "Back in 1975, folks would've said there's nothing we can do to help those babies," he said. "But now people have proven if you do heart surgery early, patients with Down syndrome can live to adulthood and be active members of their community. The difference it makes for them is tremendous." Forty percent of people with Down syndrome have congenital heart disease, Collins said. And unlike cases of trisomy 13 and 18, it is now standard-of-care to operate on children with Down syndrome.

Scientists aren't sure why trisomy 13 and 18 are associated with higher rates of congenital heart disease than trisomy 21, and why patient death rates are so much higher.

Collins is certain, however, that trisomy 13 and 18 patients have far more neurological and developmental issues than those with Down syndrome, and is unsurprised at hospitals' attitudes that surgery is considered a big risk to take with patients who have a low likelihood of survival.

Still, he suspects that the results of this study might shift the paradigm of how babies with trisomy 13 and 18 are cared for. "Surgery gives parents the option to say, 'We're going to do everything we can for our baby,'" said Collins. "And now we've shown that heart surgeries could allow parents to take their babies home from the hospital, and have them for two years or beyond, as opposed to two weeks."

Collins also said that taking care of the patients' heart problems early on could enable caregivers to then properly analyze other health issues and perform follow-up procedures, such as tracheotomies, to improve the infants' respiration. His next study, in fact, is looking at all the risk factors other than heart disease in more than 3,000 trisomy 13 and 18 patients and analyzing how their collective health problems fit together. Collins hopes eventually to create a guideline for pediatric caregivers to determine which problems to treat in which order.

His work teasing out the most effective treatments for these babies ties into 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.

Two researchers at the University of Arkansas for Medical Sciences are also co-authors.

The research did not receive external funding. The data were acquired from the Pediatric Health Information System as part of the use agreement with participating hospitals. ISM

Cancer patient receives honorary degree from her caregivers

By Erin Digitale

Three years ago, soon after Minal Patel started receiving treatment for an aggressive form of cancer, she informed her favorite oncologist at Lucile Packard Children's Hospital Stanford that she hoped to become an academic physician herself.

"I had no doubt you would do it," the physician, Emily Johnston, MD, told Patel recently. "You already had more scientific publications than I did."

Johnston, an instructor in pediatric hematology-oncology, was speaking at a ceremony held Oct. 3 in the Packard Children's auditorium to confer an honorary medical degree on 26-year-old Patel. Earlier this year, Patel's cancer relapsed; her prognosis is poor. The surprise ceremony was a way for her caregivers to acknowledge that, although Patel cannot pursue her dream of becoming a physician, she has contributed to medicine by sharing her insights into what it's like to be a young adult with cancer. Patel's mother, Priti Patel, and about 30 hospital staff members attended the celebration.

When Patel was diagnosed in 2014 with rhabdomyosarcoma, a rare, soft-tissue tumor, she was referred to Packard Children's for treatment. The tumor usually strikes kids and teenagers, so although Patel was then 23, she needed pediatric care. Rhabdomyosarcoma specialist Sheri Spunt, MD, professor of pediatrics in hematology and oncology, began working with Patel and Johnston, then a pediatric oncology fellow, to plan an intensive year of chemotherapy.

Patel told her physicians how her diagnosis had interrupted her path to medical school. She had earned a bachelor's degree in biology at the University of California-San Diego, where she worked as a research associate and co-authored the scientific papers that Johnston mentioned. She also was studying for her Medical College Admissions Test. She was eager to finish chemotherapy and return to her academic ambitions.

ERIN DIGITALE

Minal Patel (center) was presented with an honorary medical diploma at Lucile Packard Children's Hospital Stanford after her cancer relapsed, derailing her plans to study medicine. Her care team includes (from left) nurse practitioner Nichole Mosher, pediatric oncologist Emily Johnston, pediatric oncologist Sheri Spunt and nurse practitioner Pam Simon.

During her treatment, Patel became close to her caregivers, especially Johnston. "She's one of those rare physicians who keeps a physician-patient relationship and adds a friendship aspect to it," Patel said. The two discussed cancer, but also talked about many elements of their daily lives. Their relationship increased Patel's confidence that she was being treated as a person, not just a patient, and boosted her ability to have a positive outlook about her situation.

When Patel was diagnosed, Johnston was only two months into her pediatric oncology fellowship. Their close doctor-patient connection has meant a lot to her, too.

"Minal is just so fun and feisty; I always come out of her [hospital] room with a smile on my face," Johnston said. The two have bonded over their shared love of soccer. Their medical discussions include a lot of give and take; Patel once told Johnston she wished she'd been warned that her hair would always be different after chemotherapy, for example. "I'm learning how to be a pediatric oncologist," Johnston said. "I really appreciate that she is thoughtful and reflects on what's going on."

When Patel finished her planned year of treatment in August 2015, Johnston and Spunt helped celebrate. They thought she was headed for a stellar medical career. "She would be a phenomenal doctor — she's so passionate, compassionate and intelligent," Johnston said.

But early this year, the cancer relapsed. Patel resumed chemotherapy, and she and Johnston See DEGREE, page 3

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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

Conference advocates for more female leadership in global health

By Ruthann Richter

Six weeks ago, World Bank president Jim Yong Kim, MD, tweeted a photo of top leaders of the World Health Organization. It showed a group of men in business suits seated around a large table.

Michele Barry, MD, director of Stanford's Center for Innovation in Global Health, displayed the photo on a large screen. "Where are the women?" she said to a crowd of nearly 400 people — mostly women — Oct. 12 at Stanford's Li Ka Shing Center for Learning and Knowledge.

"We are here," a chorus of female voices in the crowd responded.

So began the inaugural Women Leaders in Global Health conference, designed to highlight the accomplishments of women in the field and empower the next generation of leaders to fill the gap of women at the top.

Barry noted that some 90 percent of health care around the globe occurs at home, mostly by female caregivers. "On the frontline, at least 75 percent of the health workforce are women, and looking around this room, there is no shortage of women in the pipeline," she said.

Few women at highest echelons

Yet there are few women at the highest echelons. Most health administrators, health-sector CEOs, deans, ministers of health and members of the World Health Assembly are men. And they are making critical decisions that impact the health of women around the world.

"When we have diversity, careers prosper, companies flourish and health outcomes improve," Barry said. "We all win."

ROD SEARCEY

(Top) Stanford Provost Persis Drell addressed the inaugural Women Leaders in Global Health conference. (Bottom) Susan Chira, a senior correspondent and editor on gender issues for *The New York Times*, interviewed Harriet Mayanja-Kizza, dean of medicine at Uganda's Makerere University, at the conference.

Stanford Provost Persis Drell, PhD, told the group, "Quite simply, we won't get the right answers without women in leadership roles."

The conference was held with the aim of beginning a movement for change. It featured some 400 female leaders from 68 countries, representing 250 universities, companies and nonprofits.

Harriet Mayanja-Kizza, MD, dean of medicine at Uganda's Makerere University, noted that in her sub-Saharan country, nearly all the bedside care is provided by women, whether they're nurses in hospitals or family members at home.

"I have had people tell me it's better for the wife to outlive the husband because the wife can look after him," she told the audience. "If the wife is sick, she has to find a sister or an aunt to take care of her."

Yet women in Uganda are not encouraged to join the medical profession or the sciences. She said that when she went to medical school, only 8 percent of the students were women; now it's 30 percent. Yet, she said, "Women have many things pulling against them," including the fact that many girls drop out of school by the age of 12 and are urged into early marriage and childbirth. Those who do make it into higher education have to balance family demands; one graduate student told her she was due to give birth the day her classes began. She had employed a caregiver who could sit by a tree outside to look after her baby so that she could occasionally leave class to feed the child.

Earlier this year, Sania Nishtar, MD, a Pakistani cardiologist and activist, was short-listed as a nominee to be director-general of the World Health Organization. She was the only woman on the list. During the campaign for the position, she said she visited dozens of countries.

"Women's leadership was not on the agenda of most governments," Nishtar said. "There were very few that talked about appropriate gender representation. That is a mindset that clearly needs to change."

'A lot to gain'

Men have a role to play as well through programs that mentor women and promote them as role models, said Peter Piot, MD, director of the London School for Hygiene and Tropical Medicine.

"There's the reality that in order to achieve gender parity, men have to give up something," Piot said. "But it will be better for them ultimately."

Gary Darmstadt, MD, professor of pediatrics and associate dean for maternal and child health at Stanford, agreed. "Where you have greater gender equity, men's longevity improves, as does women's longevity," he said. "So I think we have a lot to gain."

Toward the end of the daylong conference, the participants talked about concrete actions for change and received advice from some distinguished panelists on how to become "change agents."

Peru's former minister of health Patricia Garcia, MD, PhD, MPH, said women seeking to advance in the global health field should be persistent and passionate and be willing to speak up and be open to unexpected opportunities. That is, in essence, the story of her own career.

Garcia was the dean of the School of Public Health at Peru's Cayetano Heredia University in 2016 when she received a surprising call from the country's president, she said. The president invited her to his home, and after they talked, he offered her the country's top health job.

"I thought it was an opportunity to make a difference in my country, although I knew the average time of a minister in my country was six months," she said, speaking rapid-fire and with hand flourishes. "I have to tell you it was really tough, really tough. There was a lot of politics and corruption," which she said she fought against.

Still, Garcia said she managed to make some headway, increasing access to human papilloma vaccination by 85 percent, introducing telemedicine and electronic medical records and raising the salaries of health workers, among other initiatives. She lasted a year and two months in the job before the president's entire cabinet resigned in September 2017 and she returned to the university. In the process, though, she said she learned a great deal, offering this advice to the audience:

ROD SEARCEY

Michele Barry noted that some 90 percent of health care around the globe occurs at home, mostly by female caregivers.

"You have to work with passion, and you have to love what you do, and I do love public health. Do your best to create opportunities. That's why I jumped into the ministry of public health, though everybody thought I was crazy — though I call it passionate crazy. And fight against your own fears. Raise your voice when you need it. That's what I learned. And be honest. Be perseverant and also have patience because change takes time."

After her talk, Donna Shalala, PhD, former U.S. secretary for health and human services and the panel's moderator, offered a lighthearted suggestion: "You know, Patty, the United States has an opening for a minister of health," she said.

The conference was sponsored by 18 organizations.

The London School for Hygiene and Tropical Medicine has agreed to host the next conference in 2018. Patricia Garcia and Agnes Binagwaho, MD, PhD, former Minister of Health for Rwanda, also have offered to host future conferences, Barry said. **ISM**

Degree

continued from page 2

planned how she could get the most out of her remaining time. Fulfilling a soccer-fan dream, Patel attended a Real Madrid game in Spain earlier this year.

But there was another goal Patel worried she wouldn't be able to reach.

"Minal is upset because she doesn't think she will have the impact she wanted to have," Johnston said. Recalling that Patel had once expressed a wish to receive an honorary medical degree, Johnston began working with nurse practitioner Pam Simon, program manager of the Stanford Adolescent and Young Adult Cancer Program, to plan a ceremony. As she presented the diploma (inscribed to *Minal Patel, MD*) Johnston described how much her patient had taught her, and how broadly she'd affected the dozens of people in the room, and many others who had also wanted to attend.

There were a few tears during the ceremony, but much more laughter.

"Now that I'm a doctor, do I get a job offer?" Patel asked the audience, honorary diploma in hand. "I don't need a fellowship; I already went through it," she added, to chuckles from the crowd.

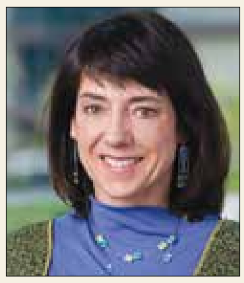
Soon everyone was offering Patel congratulatory hugs, balloons and flowers. They were eating cupcakes and snapping photos of the honoree in her academic gown. Patel kept flashing her enormous grin.

The next day, she reflected on what the ceremony meant for her. "It's the acts of kindness that remind me of the goodness of the present and people," she said. "Even in this very dark phase of cancer, there's still brightness to it." **ISM**

Scientists seek to speak the brain's language to heal its disease

By Nathan Collins

Since the 19th century at least, humans have wondered what could be accomplished by linking our brains — smart and flexible but prone to disease and disarray — directly to technology in all its cold, hard precision. Writers of the time dreamed up intelligence enhanced by implanted clockwork and a starship controlled by a transplanted brain.



Helen Bronte-Stewart

While these remain inconceivably far-fetched, the melding of brains and machines for treating disease and improving human health is now a reality. Brain-machine interfaces that connect computers and the nervous system can now restore rudimentary vision in people who have lost the ability to see, treat the symptoms of Parkinson's disease and prevent some epileptic seizures. And there's more to come.

But the biggest challenge in each of those cases may not be the hardware that science-fiction writers once dwelled on. Instead, it's trying to understand, on some level at least, what the brain is trying to tell us — and how to speak to it in return. Like linguists piecing together the first bits of an alien language, researchers must search for signals that indicate an oncoming seizure or where a person wants to move a robotic arm. Improving that communication in parallel with the hardware, researchers say, will drive advances in treating disease or even enhancing our normal capabilities.

Early days

The scientific interest in connecting the brain with machines began in earnest in the early 1970s, when computer scientist Jacques Vidal embarked on what he called the Brain Computer Interface project. As he described in a 1973 review paper, it comprised an electroencephalogram, or EEG, for recording electrical signals from the brain and a series of computers to process that information and translate it into some sort of action, such as playing a simple video game. In the long run, Vidal imagined brain-machine interfaces could control "such external apparatus as prosthetic devices or spaceships."

Although brain-controlled spaceships remain in the realm of science fiction, the prosthetic device is not. Stanford researchers, including Krishna Shenoy, PhD, professor of electrical engineering, and Jaimie Henderson, MD, professor of neurosurgery, are bringing neural prosthetics closer to clinical reality. Over the course of nearly two decades, Shenoy, the Hong Seh and Vivian W. M. Lim Professor, and Henderson, the John and Jene Blume-Robert and Ruth Halperin Professor, developed a device that, in a clinical research study, gave people paralyzed by accident or disease a way to move a pointer on a computer screen and use it to type out messages. In similar research studies, people were able to move robotic arms with signals from the brain.

Reaching those milestones took work on many fronts, including developing the hardware and surgical techniques needed to physically connect the brain to an external computer.

But there was always another equally important challenge, one that Vidal anticipated: taking the brain's startlingly complex language, encoded in the electrical and chemical signals sent from one of the brain's billions of neurons on to the next, and extracting messages a computer could understand. On top of that, researchers like Shenoy and Henderson needed to do all that in real time, so that when a subject's brain signals the desire to move a pointer on a computer screen, the pointer moves right then, and not a second later.

One of the people to whom that challenge fell was Paul Nuyujukian, MD, PhD, now an assistant professor of bioengineering and of neurosurgery. First as a graduate student with Shenoy's research group and then a postdoctoral scholar with the lab jointly led by Henderson and Shenoy, Nuyujukian helped to build and refine the software algorithms, termed decoders, that translate brain signals into cursor movements.

Actually, "translate" may be too strong a word — the task, as Nuyujukian put it, was a bit like listening to 100 people speaking 100 different languages all at once and then trying to find something, anything, in the resulting din one could correlate with a person's intentions. Yet as daunting as that sounds, Nuyujukian and his colleagues found some ingeniously simple ways to solve the problem, first in experiments with monkeys. For example, Nuyujukian and fellow graduate student Vikash Gilja showed that they could better pick out a voice in the crowd if they paid attention to where a monkey was being asked to move the cursor.

"Design insights like that turned out to have a huge impact on performance of the decoder," said Nuyujukian, who is also a member of Stanford Bio-X and the Stanford Neurosciences Institute. In fact, it more than doubled the system's performance in monkeys, and the algorithm the team developed remains the basis of the highest-performing system to date. Nuyujukian went on to adapt those insights to people in a clinical study — a significant challenge in its own right — resulting in devices that helped people with paralysis type at 12 words per minute, a record rate.

L.A. CICERO / STANFORD NEWS SERVICE

Paul Nuyujukian has helped to build and refine the software algorithms that translate brain signals into cursor movements.

Although there's a lot of important work left to do on prosthetics, Nuyujukian said he believes "there are other very real and pressing needs that brain-machine interfaces can solve," such as the treatment of epilepsy and stroke — conditions in which the brain speaks a language scientists are only beginning to understand.

Listening for disease

Indeed, if one brain-machine interface can pick up pieces of what the brain is trying to say and use that to move a cursor on a screen, others could listen for times when the brain is trying to say something's wrong.

One such interface, called NeuroPace and developed in part by Stanford researchers, does just that. Using electrodes implanted deep inside or lying on top of the surface of the brain, NeuroPace listens for patterns of brain activity that precede epileptic seizures and then, when it hears those patterns, stimulates the brain with soothing electrical pulses.

Learning to listen for — and better identify — the brain's needs could also improve deep-brain stimulation, a 30-year-old technique that uses electrical impulses to treat Parkinson's disease, tremor and dystonia, a movement disorder characterized by repetitive movements or abnormal postures brought on by involuntary muscle contractions, said Helen Bronte-Stewart, MD, professor of neurology and neurological sciences.

Although the method has proven successful, there is a problem: Brain stimulators are pretty much always on, much like early cardiac pacemakers. Although the consequences are less dire — the first pacemakers "often caused as many arrhythmias as they treated," Bronte-Stewart, the John E. Cahill Family Professor, said — there are still side effects, including tingling sensations and difficulty speaking. For cardiac pacemakers, the solution was to listen to what the heart had to say and turn on only when it needed help, and the same idea applies to deep brain stimulation, Bronte-Stewart said. To that end, "we're developing brain pacemakers that can interface with brain signaling, so they can sense what the brain is doing" and respond appropriately.

The challenge is much the same as in Nuyujukian's work, namely, to try to extract useful messages from the cacophony of the brain's billions of neurons, although Bronte-Stewart's lab takes a somewhat different approach. In one recent paper, the team focused on one of Parkinson's more unsettling symptoms, "freezing of gait," which affects around half of Parkinson's patients and renders them periodically unable to lift their feet off the ground.

Bronte-Stewart's question was whether the brain might be saying anything unusual during freezing episodes, and indeed it appears to be. Using

Planned research building designed for innovation, collaboration

By Ruth Schechter

In 1959, when the School of Medicine relocated from San Francisco to a new complex on the university campus, a gallon of gas was 25 cents, Alaska became the 49th state, Doris Day ruled the radio waves and Barbie hit toy stores.

Designed by Edward Durell Stone, the complex integrated outdoor and interior landscapes, with pierced grills, walls of glass bricks and a network of courtyards. But the buildings that compose the complex have not kept up with the accelerating demands of today's medicine, and while the recent addition of structural steel frames to the exterior of the Edwards building makes it seismically safe, the buildings remain functionally deficient.

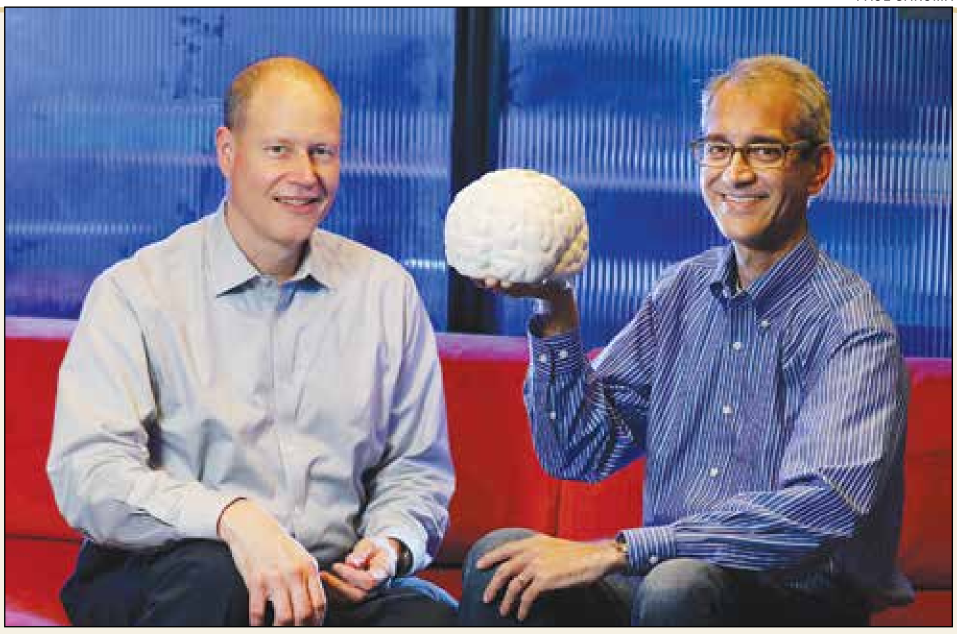
"Our labs were designed in the year Sputnik went up and built during the Eisenhower administration," said Robert Jackler, MD, professor and chair of otolaryngology-head and neck surgery. "Needless to say, our needs have changed. Our labs are scattered and out of date. The long-term sustainability of our research mission clearly requires additional space. It's time to decant the building. The complex is at the end of its usefulness."

The Biomedical Innovation See BUILDING, page 5

ZGF ARCHITECTS

The Biomedical Innovation Building will be the first in a series of new buildings that replace the Grant, Alway, Lane and Edwards buildings.

PAUL SAKUMA



Jaimie Henderson and Krishna Shenoy are part of a consortium working on an investigational brain-machine interface.

methods originally developed in physics and information theory, the researchers found that low-frequency brain waves were less predictable, both in those who experienced freezing compared with those who didn't, and, in the former group, during freezing episodes compared with normal movement. In other words, although no one knows exactly what the brain is trying to say, its speech — so to speak — is noticeably more random in freezers, the more so when they freeze.

By listening for those signs, well-timed brain stimulation may be able to prevent freezing of gait with fewer side effects than before, and one day, Bronte-Stewart said, more sophisticated feedback systems could treat the cognitive symptoms of Parkinson's or even neuropsychiatric diseases, such as obsessive compulsive disorder and major depression.

'We need to talk to those neurons'

Both Nuyujukian and Bronte-Stewart's approaches are notable in part because they do not require researchers to understand very much of the language of the brain, let alone speak that language. Indeed, learning that language and how the brain uses it, while of great interest to researchers attempting to decode the brain's inner workings, may be beside the point for some doctors and patients whose goal is to find more effective prosthetics and treatments for neurological disease.

But other tasks will require greater fluency, at least according to E.J. Chichilnisky, PhD, professor of neurosurgery and of ophthalmology, who thinks speaking the brain's language will be essential when it comes to helping the blind to see. Chichilnisky, the John R. Adler Professor, co-leads the NeuroTechnology Initiative, funded by the Stanford Neuroscience Institute, and he and his lab are working on sophisticated technologies to restore sight to people with severely damaged retinas — a task he said will require listening closely to what individual neurons have to say, and then being able to speak to each neuron in its own language.

The problem, Chichilnisky said, is that retinas are not simply arrays of identical neurons, akin to the sensors in a modern digital camera, each of which corresponds to a single pixel. Instead, there are different types of neurons, each of which sends a different kind of information to the brain's vision-processing system.

"We need to talk to those neurons," Chichilnisky said. To do that, a brain-machine interface needs to figure out, first, what types of neurons its individual electrodes are talking to and how to convert an image into a language those neurons — not us, not a computer, but individual neurons in the retina and perhaps deeper in the brain — understand. Once researchers can do that, they can begin to have a direct, two-way conversation with the brain, enabling a prosthetic retina to adapt to the brain's needs and improve what a person can see through the prosthesis.

"A one-way conversation sometimes doesn't get you very far," Chichilnisky said. ISM

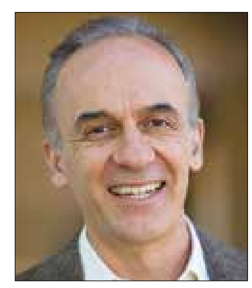
Researchers opine on wisdom of enhancing brain with tech

By Nathan Collins

Despite obvious benefits for people with otherwise untreatable conditions, there could be downsides to brain-machine interfaces being developed to treat disease or drive prosthetic limbs. As researchers get better at building interfaces and understanding the language of the brain, the possibility arises that science could enhance our senses and even our intelligence.

"There is a very blurry line between restoring and enhancing."

E.J. Chichilnisky, PhD, professor of neurosurgery and of ophthalmology, says we should pursue ever more sophisticated brain-machine interfaces regardless. Chichilnisky co-leads the Stanford Neuroscience Institute's NeuroTechnology Initiative, and in his own research is working on sophisticated, adaptive technologies to help people with severely damaged retinas. The idea is to decode a patient's visual system, then send it carefully orchestrated signals that would allow them to see not just flashes of light, as current systems can, but detailed, high-resolution images.



E.J. Chichilnisky

Such technologies could easily enhance as well as restore sight — in fact, it's almost hard not to, Chichilnisky said. The light-sensing devices in artificial retinas, known as CMOS chips — the same ones used in modern digital cameras — turn out to be so sensitive to infrared light that camera designers need to add filters to make them work properly. In that sense, it may actually take less work to enhance human vision than to restore normal vision.

William Newsome, PhD, professor of neurobiology and director of the Stanford Neurosciences Institute, said that brain-machine interfaces may add new dimensions to longstanding debates about the ethics of medical research with patients as subjects.

"Our brains are highly evolved for life on this planet," and they reflect a number of tradeoffs between, for example, the ability to learn quickly and the ability to take a long view and plan for the future, Newsome said, and fiddling with that balance could lead to negative unintended consequences.

That could be especially worrisome given Silicon Valley's enthusiasm for "hacking the brain," Newsome said, and the push to create brain-machine interfaces on the part of private companies such as Neuralink, billionaire Elon Musk's effort to enhance human intelligence, and Kernel, a similar endeavor toward cognitive enhancement. If those companies, some of which are focused on brain enhancement, make mistakes in the rush to market, it could hurt scientists doing slower, more careful work, Newsome said.

"There is a very blurry line between restoring and enhancing," Chichilnisky said, but "we are going to go there. That's what humanity does." While there have always been both good and bad outcomes of radical technological development, the net result has been mostly positive, and the human condition continues to improve as a result, he said.

Others take a somewhat more pragmatic view. "At one point I would have told you absolutely there's no way we should be trying for enhancement. We need to focus on restoring function for people who have lost it, and that's still my primary focus," said Jaimie Henderson, MD, professor of neurosurgery.

Now, "I can see the advantage of thinking a little bit beyond that and saying, if we aim for enhancement, maybe by asymptotically approaching that point, we can get closer to actual restoration," which, Henderson said, should always be the goal.

Chichilnisky is the John R. Adler Professor. Newsome is the Harman Family Provostial Professor and Vincent V. C. Woo Director of the Stanford Neurosciences Institute. Henderson is the John and Jene Blume-Robert and Ruth Halperin Professor. Each is a member of Stanford Bio-X and the Stanford Neurosciences Institute. ISM

Building

continued from page 4

Building is the first step in a sequence of new buildings that eventually will replace the outdated complex, which includes the Grant, Alway, Lane and Edwards buildings. The BMI Building will be designed to encourage interdisciplinary studies and quickly move biomedical research into clinical practice.

'Creating a contemporary environment'

The 215,500-square-foot structure will be located on open space along Pasteur Drive, just steps from the medical school's research buildings and the new Stanford Hospital. With four floors above ground and one below, the building will be a significant step toward replacing outdated research facilities and easing the space crunch. It will house laboratories and support space for nearly 1,000 faculty, students and staff in specialties that include orthopedic surgery, pediatrics, immunology and genomics.

"The BMI will bring together world-leading research teams in a modern and technologically advanced facility," said Lloyd Minor, MD, dean of the School of Medicine. "More than that, the BMI will foster scientific collaboration and encourage the formal and informal interactions that are necessary for innovation and precision health."

The building, which is scheduled for completion by 2019, will bring together multidisciplinary teams of engineers, basic scientists and physician-researchers from nine areas, including the Sean N. Parker Center for Allergy and Asthma Research; the Stanford Initiative to Cure Hearing Loss; the Stanford Cardiovascular Institute; the Stanford Human Systems Immunology Center; and the Stanford Institute for Immunity, Transplantation and Infection.

Open spaces

The building's central concept is to foster collaboration and interaction through open lab configurations and spaces that enable occupants to gather, confer and mingle. Each floor will include adaptable conference rooms, small huddle booths and open lounge areas. An 80-seat meeting room and a large outdoor terrace will be accessible for scientific symposia and receptions.

Niraj Dangoria, associate dean for facilities planning and management at the medical school, said the building integrates lessons learned from the design of the school's previous research buildings. Dispersed throughout the floor plan are areas for formal and informal interactions, a feature especially important for encouraging collaboration among the scientists and physicians.

"The new building will help build stronger institutes and departments because of the enhanced interconnectivity and new facilities," said Jackler, who worked with the architects to help refine the plans. "The co-location of researchers will increase scientific synergy. Not only will we take steps to address the research space crisis in the medical school, we will have modern laboratory space with better connectivity of shared interests and technologies."

Each floor will house shared laboratory space arranged in color-coded zones for traditional research activities, as well as for "dry" research that leverages Stanford's strengths in computational science and big data. Oversized windows will ensure lots of natural light and offer expansive views of the medical campus. The contemporary design will integrate the highest standards of sustainability and environmental concerns and reflect best practices for laboratory design safety and space allocation.

"We are planning to accommodate the needs of researchers for many years to come, so the building's infrastructure needs to be flexible and adaptable," Dangoria said. "Technologies are changing, and finding contiguous space to grow continues to be a challenge. Faculty, fellows and students require spaces that encourage collaborative, multidisciplinary efforts, so we approached the design to inspire ways for different disciplines to work together on basic, translational and clinical studies." ISM

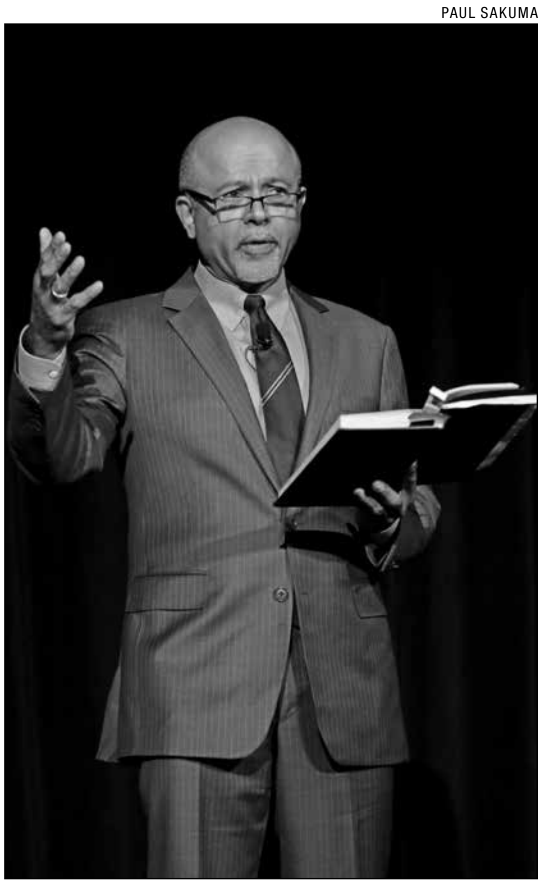
Burnout

continued from page 1

Noting that while perfectionism "can get people into the medical profession," she said that "it can be toxic when paired with a belief system of being hard on yourself."

Self-compassion is more than just pampering yourself, she said; it's allowing yourself to receive compassion from others: "Self-compassion means opening yourself to the compassion that's available to you."

PAUL SAKUMA



Author and physician Abraham Verghese discussed physician suicide at the conference.

"This is a skill that you can actually practice," she said, offering examples such as meditating on connections with others, celebrating self-care, accepting condolences and remembering that no one is alone in suffering. Research has shown that such practices can decrease burnout, she said.

The right leadership

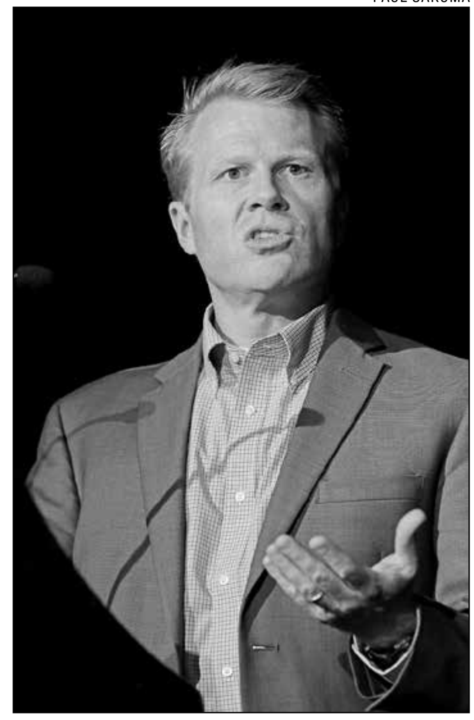
Creating a culture in health care organizations that encourages physicians' well-being starts with placing the right people in leadership positions, said Vivek Murthy, MD, a former U.S. surgeon general. Organizations should hire people for the way they treat others, he said, not for their ability to win a Nobel Prize. "Kindness is spread more quickly than infectious diseases," he said.

The Mayo Clinic studied the factors that affected physician satisfaction and found that good supervisors were critical, added Shanafelt, who came to Stanford this year from Mayo. It came down to "Leadership 101," he said: "communication, appreciation, asking opinions and facilitating career development."

After developing leadership skills and instituting practices such as regular colleague meetings, Mayo saw burnout levels drop. "As the national numbers continued to worsen, Mayo was able to reverse the trend," he said.

EHRs take much of the blame for physician dissatisfaction, but better systems will ultimately reduce the administrative burden, said Robert Wachter, MD, chair of medicine at UC-San Francisco. Nearly all health care organizations have gone digital in less than 10 years, he said: "It's a huge, huge transformation in a relatively short period of time."

PAUL SAKUMA



Tait Shanafelt, director of the Stanford WellMD Center, said physician burnout can contribute to cynicism among other members of the care team.

"There's an infectious component of burnout."

The kinks are still being worked out, he added. Many EHRs, for example, prompt caregivers to ask repeated, pointless questions. "The EHR is creating a huge amount of silly work for well-trained people," he said.

Over time, he asserted, the EHR will improve, much the way smartphones have become easier to use. "Eventually, productivity gets better," he said.

Christine Sinsky, MD, vice president of professional satisfaction at the American Medical Association, said organizations can save three to five hours a day of physicians' work time by simply re-engineering practices. She provided an example of a physician whose two medical assistants take care of the administrative work. They accompany him to patient rooms, where they type information into the EHR; they also renew prescriptions and retrieve lab results.

A few simple equipment fixes — such as using card readers instead of requiring passwords, and having printers in patient rooms — can also shave time off a physician's day, Sinsky added.

"We have physicians and nurses spending hours and hours per week that do not add value to the patient," she said.

But Minor said that using medical assistants and scribes, who remotely transcribe conversations between patients and doctors, is "at best an intermediate step." A better solution, he said, is to "design front ends that make workflow more efficient."

Ultimately, improving physicians' well-being will require a number of changes to the practice of medicine, with input from all parties. "We need to get our communities to help us," Minor said, "and be intentional about involving everyone in our organization." ISM

GTEx

continued from page 1

ourselves, from our eye or hair color, to our height and shape and even our likelihood of developing various diseases.

But interpreting exactly which, and how, each of those differences bring about these outcomes has been difficult, particularly when the genetic differences occur not in the coding regions of genes, but instead in the surrounding regulatory regions that control their expression.

Furthermore, some genes are expressed only in particular tissue types and not others, making them challenging to study.

In 2010, scientists from around the country banded together at the urging of the National Institutes of Health to better understand how variations in an individual's DNA sequence affect whether, where, how and when specific genes are expressed in tissues throughout the body. The collaborative effort, known as the Genotype-Tissue Expression, or GTEx Project, aims to learn at the most basic level how and why individuals differ. The knowledge is likely to transform our understanding of disease and eventually change the way medicine is practiced, researchers believe.

"Until now we didn't know in which tissues these variants exerted their effects."

"We've known for years that certain genetic variants confer increased risk for a variety of diseases," said Stephen Montgomery, PhD, assistant professor of pathology and of genetics at the School of Medicine, "but until now we didn't know in which tissues these variants exerted their effects. As genes vary in their levels of expression or activity among the many tissues of the human body, we've now been able to identify where variants exerts their effects and connect this variation to complex human traits and diseases."

The project is supported by the National Institute of Health's Common Fund, which is meant to address challenging, high-priority biomedical problems outside the scope of any one institute alone, but that, when solved, will benefit researchers throughout the field. Researchers from 30 institutions across the country and around the world collaborated as part of the GTEx consortium over the past seven years.

The culmination of the GTEx Project is described in a series of eight papers that were published Oct. 12 in *Nature*, *Nature Genetics* and *Genome Research*. The papers show how small variations in an individual's genome sequence govern the expression levels of genes in 44 distinct human tissues. Researchers at Stanford — including Montgomery; professor of genetics Michael Snyder, PhD; and assistant professor of genetics Jin Billy Li, PhD — are the senior or co-senior authors of four of the eight papers, along with researchers from Johns Hopkins University, the University of Pennsylvania, Princeton University, the University of Chicago and MIT's Broad Institute.

Jin Billy Li

Michael Snyder

Stephen Montgomery

Moving beyond sequencing

GTEx researchers correlated the genetic variation of more than 7,000 samples from 449 cadaver donors with gene expression levels in 44 tissues, including brain, muscle, liver and blood. They found that most genes vary in their levels of expression among an individual's tissues and that the levels of expression are affected by specific variants in each individual's genome sequence.

Montgomery shares senior authorship of the core GTEx paper in *Nature,* which correlates the effect of genetic variants with tissue-specific gene expression, with three other researchers from Johns Hopkins, Penn and Princeton. He is the co-senior author of another *Nature* paper investigating the effect of rare genetic variants, which are difficult to study in conventional genetic studies. That study showed that nearly 90 percent of individuals displaying abnormally high or abnormally low levels of gene expression in particular tissues have rare variants near the affected genes.

Li is the senior author of a third paper in *Nature* investigating how RNA editing — a mechanism to modify genomically encoded nucleotides in the RNA, thus giving rise to important cellular functions — varies among tissues and species, including humans, mice and primates.

"We learned that RNA editing is tissue-specific and developmental stage-specific and dynamically regulated," said Li, "but its patterns are more similar within all the tissues of one species than in one type of tissue across species. This is the most comprehensive atlas of RNA editing in tissues and species and will provide a valuable resource for many researchers. Our analyses already led to unexpected, novel insights of the dynamic regulation of RNA editing."

The Enhancing GTEx Project

Finally, Snyder and Montgomery share co-senior authorship with researchers from the Broad Center and the University of Chicago of a paper in *Nature Genetics* that announces the formation of a new project of NIH's Common Fund called the Enhancing GTEx Project. This effort will work to link the GTEx findings with other tissue-specific molecular data, including DNA methylation patterns, levels of protein expression and telomere length.

"These studies will allow us to understand the differences among individuals at a level that has never before been achieved," said Snyder. "These differences manifest themselves as molecular signatures that will ultimately enable us to better treat many human diseases."

Montgomery is a member of Stanford Bio-X and the Stanford Child Health Research Institute. Snyder is the chair of Stanford's Department of Genetics and directs Stanford's Center for Genomics and Personalized Medicine. He is a member of Bio-X, the Child Health Research Institute, the Stanford Cardiovascular Institute, the Stanford Cancer Institute and the Stanford Neurosciences Institute. Li is a member of Bio-X and the cardiovascular, cancer and neurosciences institutes.

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

▪ OBITUARY

John Freidenrich, Stanford leader and donor, dies at 80

By Alex Shashkevich

Prominent Stanford leader and donor John Freidenrich, an alumnus who was involved with the university for more than 40 years, died Oct. 11 at Stanford Hospital. He was 80.

Freidenrich, who was a successful lawyer and venture capitalist, served as chair of the university's board of trustees and on the boards of directors of Stanford Hospital and Lucile Packard Children's Hospital. In addition, he and his wife, Jill, actively supported many initiatives at Stanford throughout his life.

"John was a beloved and cherished friend to many of us at Stanford University and at Stanford Health Care," wrote Stanford President Marc Tessier-Lavigne, PhD, and board of trustees chair Jeffrey Raikes in a statement informing the Stanford community of the news. "John combined decades of distinguished volunteer leadership at Stanford University and Stanford Medicine with exemplary stewardship and invaluable counsel."

John Freidenrich

A life of generosity

Freidenrich's generosity and commitment to Stanford spanned the tenures of four university presidents and more than 40 years.

In the 1970s, he and Jill, a Stanford alumna, began providing funding and helped raise money to support a range of university priorities, from athletics and undergraduate scholarships to law, art and medicine. The couple met while they were students at Stanford.

In the late 1980s, Freidenrich was a national co-chair of the major gifts committee of Stanford's five-year Centennial Campaign, which raised nearly $1.3 billion. After the 1989 Loma Prieta earthquake damaged the Cantor Arts Center, John and Jill Freidenrich contributed money to rebuild the center and endow its directorship. The couple was also part of the capital funding campaign that helped create Lucile Packard Children's Hospital, founded in 1991.

Most recently, in October 2012, Stanford Medicine opened the Jill and John Freidenrich Center for Translational Research, created with a $25 million donation from the couple, to conduct research that translates basic science discoveries into treatments and diagnostics. The concept for the center was inspired by Jill Freidenrich's own experience. She survived breast cancer after being diagnosed in 1991.

"Stanford is one of the few places where this is possible," John Freidenrich said in a 2011 interview of the couple's efforts in helping drive the future of medicine. "There are many talented people in different disciplines all on one campus. They are bright, tireless and collaborative, and once they get together, incredible things happen."

Aside from donating money, Freidenrich also donated his time through volunteering and serving in various leadership positions at the university.

Between 1984 and 1992, Freidenrich served on the boards of directors at Stanford Hospital and Lucile Packard Children's Hospital. He was a member of the university's board of trustees for a decade, serving as chair between 1992 and 1996. He also served on numerous other university boards, including those of the Law School, the School of Medicine and the Stanford Institute for Economic Policy Research.

In 1987, Freidenrich was awarded the Gold Spike Award for distinguished volunteer leadership service to the university by Stanford Associates, an honorary organization of alumni who have been identified as the university's top volunteers. He and Jill have been honored with the Stanford Associates' Governors' Award and Degree of Uncommon Man and Uncommon Woman, and the School of Medicine's Dean's Medal.

"As we mourn John's passing, we can be grateful for having known such an extraordinary person, perhaps best known for his selfless service and dedication and for a life well-lived with deep meaning and purpose," Tessier-Lavigne and Raikes wrote. "John showed tremendous confidence in Stanford as his alma mater, and may we honor his memory by continuing our work that he so valued in service to society."

Local resident gives back

Born in San Francisco and raised in Palo Alto, Freidenrich graduated with two degrees from Stanford — a bachelor's degree in economics in 1959 and a law degree in 1963. His father, David Freidenrich, was also an alumnus of Stanford's undergraduate program and the law school.

In 1968, John Freidenrich started the law firm of Ware & Freidenrich, which is now part of DLA Piper, focusing on the needs of start-up companies. Later, he founded the Silicon Valley venture capital firm Bay Partners and led the company for over a quarter century. Most recently, he co-founded the Regis Management Company, a multibillion-dollar portfolio manager and investment adviser, and served as the company's chairman.

Family members describe Freidenrich as a gentle, hardworking and visionary person.

"My father's accomplishments were vast and seemingly endless," said his daughter, Gail Marks, in an email. "Despite his tremendous success, he never stopped being that nice young man from his beloved and lifelong hometown of Palo Alto. He was the personification of small-town boy made good.

"His joy came from helping others. His life was one of duty and purpose and doing. Humility and kindness were his calling cards."

In lieu of flowers, the Freidenrich family asks that donations be made in his name to Stanford University for "The John Freidenrich Memorial Fund for Stanford Medicine," to the Palo Alto nonprofit Bay Area Cancer Connections and to the San Francisco-based Jewish Community Federation.

Freidenrich is survived by his wife of 54 years, Jill; children Gail Marks and Eric Freidenrich, and their spouses Andrew and Amy; his brothers David and Dennis Freidenrich; and six grandchildren: Jacqueline, Danielle, Theodore, Lucille, Beverly and Sylvia.

An event celebrating Freidenrich's life will be announced by his family at a later date. ISM

Mutation

continued from page 1

bryos can make it through development without any obvious effects, and then adult mice show greatly enhanced resistance to tumor growth."

Mice that harbored the favorable mutation, which occurred in a transcriptional activation domain called TAD2, displayed longer, pancreatic cancer-free survival than mice with normal copies of the p53 gene. Attardi's study showed that, at 400 days old, nearly 40 percent of the mice with normal p53 function had succumbed to pancreatic cancer, whereas none of the mice with the mutant form showed signs of tumor formation.

"It's not to say that mice with the mutated version of p53 would never get cancer, but this experiment suggests that this particular mutant is really potent in limiting tumor development," Attardi said.

> "What's incredible about this mutant is that it hit a sweet spot."

It turned out that the mutant hyperactivates p53, causing a subset of its downstream targets to get a surge of activity, too. But with more than 100 target genes sent into overdrive, it was critical for Attardi's team to narrow down which genes directly affected tumor suppression. Genomic data and past studies in human cancers pointed the team to the gene Ptpn14. More importantly, Ptpn14 is a known regulator of Yap, a protein that, when unchecked, turns on cancer-promoting genes in the body.

The axis of tumor super-suppression

Attardi's findings allowed her to define a pathway, or "axis," consisting of three proteins that contribute to p53-mediated tumor suppression, and it works in a linear fashion. In the chain of command, p53 ranks highest and activates Ptpn14; Ptpn14 then suppresses Yap to keep cells from turning cancerous.

In collaboration with co-author Christina Curtis, PhD, assistant professor of medicine and of genetics, and postdoctoral scholar Jose Seoane, PhD, Attardi used human cancer genomic data to extend the paradigm further, showing that when p53 is mutated in human cancer, Yap activity increases, allowing tumors to develop.

Attardi said the axis actually suggests that p53 and Ptpn14 deficiency can promote the same consequence of Yap activation.

"I think this p53-Ptpn14-Yap axis is a central mechanism," Attardi said. "P53 affects a lot of tumor-suppression processes, so if it influences a central protein like Yap, which also controls a lot of cancer processes, it can have widespread effects on cell behavior."

Attardi added that she would be hesitant to say that this is the one and only mechanism. "It would be too simplistic to think that this is absolutely the only pathway that's involved in p53-mediated suppression of pancreatic cancer, so I suspect that there will be other contributions as well."

The team's findings could inform a new type of therapeutic, mimicking the p53 super-mutant to upregulate tumor suppression. It could also inform those who are developing therapeutic Yap inhibitors.

"Clearly, Yap is a very potent oncogene," Attardi said. "And our study suggests that perhaps the focus should be on developing Yap inhibitors for tumors where p53 is gone — maybe it's more critical in those cancers."

Now, Attardi and her team are continuing to investigate whether their newly uncovered p53 mechanism holds true for a wide range of cancers, not just pancreatic.

"We want to know if this is a tissue-specific pathway and if this really is relevant for different tumor types," Attardi said. "So we're turning to experimental models to test that."

Other Stanford co-authors of the study are postdoctoral scholars Liz Valente, PhD, Nitin Raj, PhD, and Jonghyeob Lee, PhD; graduate student Brittany Flowers; life sciences researcher Jacob McClendon; research associate Kathryn Bieging-Rolett, PhD; resident Margaret Kozak, MD; Daniel Chang, MD, professor of radiation oncology; Teri Longacre, MD, professor of pathology; Albert Koong, MD, PhD, professor of radiation oncology; Seung Kim, MD, PhD, professor of developmental biology and of medicine; and Hannes Vogel, MD, professor of pathology.

Researchers at the University of Toronto and Johns Hopkins University also contributed to the work.

The research was supported by the Canadian Natural Sciences and Engineering Research Council and by the National Institutes of Health.

Stanford's departments of Radiation Oncology and of Genetics also supported the work. ISM

Panel discussion including Minor, Prober will examine compassion in health care

The practice of compassion is integral to health care, but in the bustle of busy schedules, regulatory demands and stressful environments, it can be neglected. How, then, can compassion be fostered?

That question will be the focus of an upcoming panel discussion, "Compassion in health care: Best practices by corporations, clinicians and care recipients," featuring Lloyd Minor, MD, dean of the School of Medicine; Charles Prober, MD, senior associate vice provost for health education and the founding executive director of the Stanford Center for Health Education; Dale Beatty, DNP, chief nursing officer and vice president for patient care services at Stanford Health Care; and Mickey Trockel, MD, PhD, clinical associate professor of psychiatry and behavioral science.

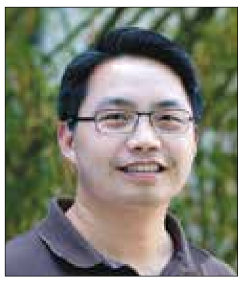
The event is part of the weeklong Contemplation by Design Summit that features efforts to promote resilience, balance, tranquility and creative excellence.

It will be held Nov. 1 from 5:45 to 7 p.m. in Dinkelspiel Auditorium on the university campus. It is free and open to the public. To reserve a seat, register at https://contemplation.stanford.edu/summit.php. ISM

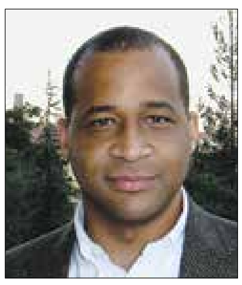
Two faculty members elected to National Academy of Medicine

Howard Chang, MD, PhD, professor of dermatology, and Tirin Moore, PhD, professor of neurobiology, have been elected members of the National Academy of Medicine.

They are among the 70 new members and 10 new international members announced Oct. 16 by the academy, which provides independent, scientifically informed analysis and recommendations on health issues.



Howard Chang



Tirin Moore

Chang is the director of the Center for Personal Dynamic Regulomes at Stanford, and the Virginia and D.K. Ludwig Professor of Cancer Genomics. His research focuses on understanding how epigenetic tags on DNA affect gene expression and coordinate cell fate and function, as well as on the role played by long noncoding RNAs and other RNA structures in biological regulation. He is a member of the Stanford Cancer Institute, the Stanford Neurosciences Institute, the Stanford Child Health Research Institute, Stanford ChEM-H and Stanford Bio-X.

Moore is a Howard Hughes Medical Institute investigator. His research focuses on neural mechanisms of sensory-motor integration and the neural basis of cognitive functions, such as attention. Work in his lab has elucidated how neural signals related to movement influence the processing of visual information by sensory neurons, and how the integration of visual and movement signals within the brain influence perception and guide behavior. He is a member of the Stanford Neurosciences Institute, the Child Health Research Institute and Bio-X.

Election to the academy recognizes individuals who have made major contributions to the advancement of the medical sciences, health care or public health. ISM

Diabetes Research Center awarded $7 million by NIH

By Tracie White

The School of Medicine has been awarded a grant from the National Institutes of Health to fund the Stanford Diabetes Research Center.

Seung Kim

The five-year, $7.7 million grant will be used to provide support for the research, training and clinical activities of the center's 90 members, which include faculty from the schools of Medicine, of Engineering and of Arts and Sciences.

With the grant, the center joins 16 other federally supported diabetes research centers nationwide.

The center's mission is to foster innovation, new knowledge and training in basic and translational diabetes-related research, leading to improved diagnosis, treatment and prevention of diabetes and its complications, said Seung Kim, MD, PhD, professor of developmental biology and director of the center, which was established last year.

"We view this as important recognition of the outstanding and enduring fundamental and clinical investigations at Stanford that focus on understanding and treating diabetes," Kim said. "Unfortunately, diabetes incidence in its major forms is increasing worldwide. So this support is timely."

Examples of ongoing research supported by the center include several projects to build an artificial pancreas, build an atlas of human pancreas cells, research the genetic basis of insulin resistance, and improve care and prevent complications in patients with Type 1 diabetes.

"Our members are united by a common interest in understanding, treating and curing diabetes, including Type 1 and Type 2 diabetes, and forms of diabetes linked to pancreatic cancer," Kim said. ISM

OF NOTE

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

HELEN BLAU, PhD, professor of microbiology and immunology, the Donald E. and Delia B. Baxter Foundation Professor and director of the Baxter Laboratory for Stem Cell Biology, was appointed by Pope Francis as an academician of the Pontifical Academy of Sciences. The academy, founded in 1603 and comprised of 70 scientists from around the world who serve for life, both Catholics and non-Catholics, advises the pope on scientific issues. She will receive an insignia of her appointment in fall 2018.

DAVID CAMARILLO, PhD, assistant professor of bioengineering, and Michael Yip, PhD, a former postdoctoral scholar, co-authored "Model-less hybrid position/force control: A minimalist approach for continuum manipulators in unknown, constrained environments," which was awarded the 2017 *IEEE Robotics and Automation Letters* Best Paper award. In addition, the paper "In vivo evaluation of wearable head impact sensors," of which Camarillo was senior author, won the Editor's Choice Award from the *Annals of Biomedical Engineering*.

SCOTT CERESNAK, MD, has been promoted to associate professor of pediatrics, effective Aug. 1. He works primarily in pediatric cardiology, with a subspecialty focus in pediatric electrophysiology and arrhythmias in adults with congenital heart disease. His research interests include signal analysis in the electrophysiology laboratory, arrhythmia syndromes in children, and arrhythmias in adults with congenital heart disease.

JAMES CHANG, MD, professor and chief of plastic and reconstructive surgery and the Johnson & Johnson Professor of Surgery, has been inducted as president of the American Society for Surgery of the Hand, the largest hand surgery organization in the world. His interests include the use of tissue engineering and microsurgery to improve clinical care for hand trauma, tendon-bone injuries and congenital hand problems.

KARL DEISSEROTH, MD, PhD, professor of bioengineering and of psychiatry and behavioral sciences, and **TONY WYSS-CORAY**, PhD, professor of neurology and neurological sciences, have been awarded NOMIS Distinguished Scientist and Scholar Awards by the NOMIS Foundation, based in Switzerland. The awards, which include $2.5 million each, support exceptional scientists who are pursuing unconventional investigations. Deisseroth, who holds the D.H. Chen Professorship, plans to use the funding to employ CAPTURE, which combines optogenetics and a technique that renders tissue transparent, to record and control thousands of neurons across the brain, with the goal of understanding the relationship between neurodynamics and behavior. Wyss-Coray will use proteomic tools and genetic approaches in the short-lived African killifish to discover and evaluate circulatory factors with the potential to rejuvenate aged or degenerated brains.

KARUNA DEWAN, MD, was appointed assistant professor of otolaryngology-head and neck surgery, effective Aug. 1. She specializes in voice, breathing and swallowing problems in adult patients, including the surgical management of dysphagia and approaches for managing chronic cough. Her research focuses on quality of life, surgical outcomes and resident education.

STEPHANIE HARMAN, MD, clinical associate professor of medicine, was named a 2017 Sojourn Scholar by the Cambria Health Foundation. The professional development program was created to support emerging leaders in palliative care. The program provides $180,000 over two years to support a palliative-care project and leadership development. Her project will focus on the use of machine learning to improve palliative care access. Her research and clinical interests include bioethics in end-of-life care and communication in serious illness. She is the clinical section chief of palliative care.

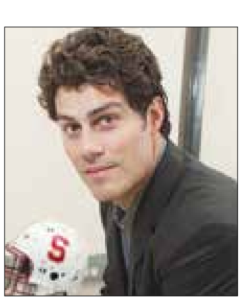
K.C. HUANG, PhD, associate professor of bioengineering and of microbiology and immunology, was named to the SN 10: Scientists to Watch list produced by *Science News*. Each scientist— age 40 or under — was nominated by a Nobel laureate or recently elected member of the National Academy of Sciences. Huang's research focuses on understanding how bacteria address physical challenges.

CARLOS MILLA, MD, was promoted to professor of pediatrics, effective Aug. 1. His interests include the inflammatory responses that lead to airway disease in cystic fibrosis and the metabolic factors that contribute to CF lung disease progression, as well as newborn screening to understand the development of lung disease in infants with CF. He directs the Stanford Cystic Fibrosis Center.

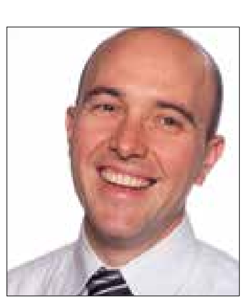
JOHN MORTON, MD, associate professor of surgery and chief of bariatric and minimally invasive surgery, has received the ASMBS Foundation's Outstanding Achievement Award from the American Society for Metabolic and Bariatric Surgery, the organization's highest honor, which includes $5,000. The award recognizes an ASMBS member with a strong commitment to the organization who has made significant contributions to the field of metabolic and bariatric surgery.

AARON NEWMAN, PhD, was appointed assistant professor of biomedical data science, effective Aug. 1. His research focuses on building data-science tools to understand the biology and clinical significance of neoplastic tissue composition. ISM

Helen Blau



David Camarillo



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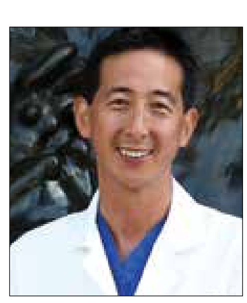

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Karl Deisseroth

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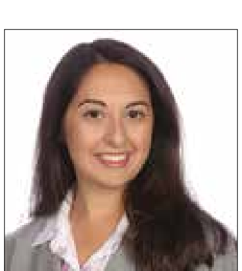

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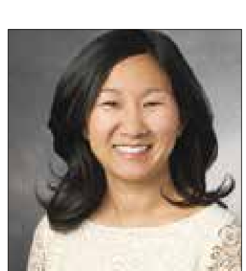
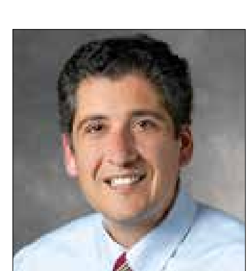


Stephanie Harman

K .C. Huang



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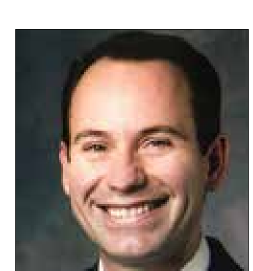
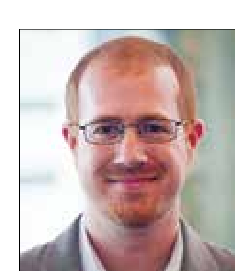


John Morton



Aaron Newman