



Clinical trial participants with Alzheimer's disease who received blood plasma from young donors showed some evidence of improvement.

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## Novel biomedical study seeks participants

By Krista Conger

Leslie Purchase describes herself as kind of a data devotee. So last spring, when she heard about the Project Baseline study — one of the largest, most comprehensive efforts to understand the basic underpinnings of health and disease — she jumped at the chance to participate.

"I'm so excited to be part of this effort to understand more about what makes the human body work," said Purchase, 41, a former physician and mother of three who volunteers with the non-profit Rotaplast International. "It's an opportunity to help inform health and wellness on a scale that's never before been attempted, and I think it's a pretty easy way to do something good for the world."

The study is an ambitious endeavor, with a potentially transformative payoff. Launched in April after years of designing and planning by Verily, an Alphabet company, in partnership with Stanford Medicine and the Duke University School of Medicine, it aims to understand the molecular basis of health by repeatedly collecting vast amounts of biomedical data from as many as 10,000 participants over the course of at least four years. Stanford Medicine recently enrolled its 100<sup>th</sup> participant in the study.

Observing how a person's health data changes over time, regardless of whether they remain healthy or fall ill, could provide the first comprehensive atlas of what



STEVE FISCH

Leslie Purchase of Mill Valley was among the first to enroll in Stanford's portion of Project Baseline. The watch on her wrist helps keep track of her activity.

it means to be "well" at all stages of life, or help researchers learn the subtle signals given off by the body at the earliest stages of cancer, heart disease or other disorders.

The scope of the effort, and its potential to eventually change how medicine is practiced by enabling physicians to proactively monitor a person's health and provide preemptive medical care

— a concept known as precision health — has captured the imagination of researchers and participants alike.

Purchase, a resident of Mill Valley, is a particularly valuable participant. See **BASILINE**, page 7

## New children's hospital, Project Baseline highlighted at State of Stanford Medicine

By Ruthann Richter

The importance of a diverse community and the politics of health care were among the topics that dominated the State of Stanford Medicine on Oct. 24.

During the lunchtime town hall meeting, the medical center's three leaders also highlighted new facilities, including the planned opening of the expanded Lucile Packard Children's Hospital Stanford, and the integrated strategic planning process, which aims to better align the priorities of the medical school, Stanford

ROD SEARCHY



Lloyd Minor, David Entwistle and Christopher Dawes spoke Oct. 24 at the State of Stanford Medicine event at the Li Ka Shing Center.

Health Care and Stanford Children's Health.

Lloyd Minor, MD, dean of the School of Medicine, kicked off the event by introducing several new initiatives at the school, including Stanford's participation in Project Baseline, a partnership with Duke University and Verily, an Alphabet company, that aims to understand the molecular basis of health by collecting vast amounts of biomedical data from as many as 10,000 participants, including 5,000 in the Bay Area, over the next four years (*see story above*).

"We should be able for the first time to get information about the predisposing factors for diseases," Minor told some 350 faculty and staff at the Li Ka Shing Center for Learning and Knowledge, where the event was held. "We're really hoping the conclusions will empower and drive our efforts in precision health — to understand the determinants of health, as well as the determinants of disease, and therefore be able to predict and prevent disease."

Minor also emphasized the importance of a diverse campus community, saying that broad representation and inclusion remain one of the school's high priorities. The newly established Diversity Center of Representation and Empowerment, at Lane Medical Library, and recent Stanford-sponsored meetings, including a conference in the spring on race, policing and public health, are helping to shine a light on the issues of diversity and inclusion and the search for solutions.

This year, 25 percent of the entering classes of both doctoral students in the biosciences and medical students are comprised of

See **MEDICINE**, page 6

## Regular marijuana use linked to more sex, according to new study

By Bruce Goldman

The jury's still out on rock 'n' roll. But the link between sex and at least one drug, marijuana, has been confirmed.

A study by investigators at the School of Medicine indicates that, despite concerns among physicians and scientists that frequent marijuana use may impair sexual desire or performance, the opposite appears more likely to be the case.

The findings, published online Oct. 27 in the *Journal of Sexual Medicine*, are based on an analysis of more than 50,000 Americans ages 25-45. And they're unambiguous.

See **MARIJUANA**, page 6

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Researchers have found a positive association between the frequency of marijuana use and the frequency of sexual intercourse.

# Ann Arvin, dean of research, to step down after 12 years

By Lisa Lapin

Ann Arvin, MD, has announced that she will step down as the vice provost and dean of research at Stanford in the fall of 2018. She will have served for 12 years in the role.

A professor of microbiology and immunology, Arvin will return to research and teaching. Provost Persis Drell, PhD, will appoint a search committee in the coming weeks and begin the process of finding a successor.

"It has been my great privilege to work with our faculty and their students as they pursue Stanford's long and valued tradition of research and scholarship in the disciplines while also addressing major societal challenges," said Arvin, who holds the Lucile Salter Packard Professorship in Pediatrics. "My primary objective has been to support the remarkably collaborative spirit that enables Stanford researchers to cross the traditional disciplinary boundaries in their search for solutions to the most fundamental research questions, and to the most pressing

problems of the global community. I am very grateful to Stanford's many knowledgeable, talented administrators, and especially our VP DoR team, who were indispensable to this effort. Having a chance to help create opportunities for faculty and students to explore their most promising ideas in an environment that facilitates their success has been a deeply rewarding experience."

Arvin has made it her chief priority to engage with faculty directors to optimize the contributions of Stanford's 18 universitywide interdisciplinary laboratories, centers and institutes, encompassing the life and physical sciences, humanities and social sciences. She placed an equal focus on the day-to-day implementation of Faculty Senate policies that embody core principles and shared values, including openness in research, academic freedom and the responsible conduct of research.

## Advocate for sound federal research policies

Throughout her service, Arvin has also represented the university nationally to advocate for sound federal research policies, serving most recently on two National Academy committees to reduce the burden of research regulations and foster research integrity at universities.

"Stanford has been extremely fortunate to benefit from Ann's deep understanding of the issues facing researchers, her strategic vision for new research avenues, and her dedicated and extensive national service in helping key federal agencies develop regulations and policies," Drell said. "Ann is one of the most respected research administrators in the country, and she has been a tremendous advocate for enabling research here at

Stanford. It is a demanding job and we are all in her debt."

The core mission of the research office is to facilitate the many diverse faculty-led research programs, which led to more than \$1.2 billion in extramural support at Stanford and SLAC National Accelerator Laboratory in 2016, through the work of seven administrative offices, together with the Office of Research Administration. Major objectives have been helping to provide state-of-the-art shared facilities that are essential for contemporary research — from research computing and nanosciences to digital humanities and the Stanford Center at Peking University, and most recently the Stanford-SLAC cryo-electron microscopy facility — and supporting the faculty and research staff who ensure the excellence of these important facilities.

Arvin's work to help forge connections between researchers throughout the university is exemplified by the growth of Stanford's interdisciplinary institutes. Her goal has been to support the dedicated efforts of the faculty directors aiming to create intellectual

and physical environments that inspire dialogue across disciplines, enhance innovation and engage faculty and trainees from all seven schools.

"Ann has viewed her role as that of a supporter to all of Stanford's research enterprise, and as an advocate to assure our researchers thrive and can easily collaborate," said Stanford President Marc Tessier-Lavigne, PhD. "She understands that Stanford's remarkable success in research lies with our innovative, creative faculty, and she has done remarkable work in enabling them to work together, across disciplines, and to be successful even within a challenging environment for research funding."

During her tenure, five interdisciplinary institutes were launched or became established programs, including the Woods Institute for the Environment, the Precourt Institute for Energy, the Stanford Center for Longevity, the Stanford Neurosciences Institute, and Chemistry, Engineering & Medicine for Human Health (ChEM-H); Spectrum, the Stanford Center for Clinical and Translational Research and Education, was established with the School of Medicine; and the Center for Advanced Study in the Behavioral Sciences joined Stanford. During this time, Bio-X, the Freeman Spogli Institute for International Studies, the Stanford Institute for Economic Policy Research, the Stanford Humanities Center, the Geballe and Ginzton laboratories, and the joint SLAC-Stanford Institute for Materials & Energy Sciences, Photon Ultrafast Laser Science and Engineering Institute, and Kavli Institute for Particle Astrophysics and Cosmology have continued to

expand their innovative programs.

These successes are owed to dynamic faculty directors and the commitment of the president, provost, and school deans and associate deans for research, as well as the development team created to support the interdisciplinary centers and institutes and their dedicated volunteer advisory councils, Arvin said.

## 'A visionary leader'

"Ann has been a visionary leader of interdisciplinary themes at Stanford," said Carla Shatz, PhD, director of Stanford Bio-X and professor of biology and of neurobiology. "She recognized the power and benefit of creating opportunities for research and training across the university long before many of our peer institutions, and she helped transform the way scientific research is being done."

Arvin has also guided key research support enterprises, including the Office of Environmental Health and Safety; the Export Control Office; the Office of Science Outreach; the Research Compliance Office, which oversees research involving human subjects and animals; and the Office of Technology Licensing. The Office of International Affairs was created under her purview.

During Arvin's tenure, new web-based tools have also been developed to aid research, including an online system for financial interest disclosures; the DoResearch site, which gives user-friendly access to policies and procedures; and the expansion of Stanford Profiles to share the research and scholarly interests and publications of faculty and trainees within and beyond the university.

Prior to assuming her role as vice provost and dean of research, Arvin served as associate dean of research from 2001 to 2006, and was chief of the infectious disease division of the Department of Pediatrics and Lucile Packard Children's Hospital from 1984 to 2006.

Arvin received her bachelor's degree in philosophy from Brown University, her master's degree in philosophy from Brandeis University and her medical degree from the University of Pennsylvania in 1972. She completed her pediatrics residency at the University of California-San Francisco, and subspecialty training in infectious diseases at UCSF and Stanford.

Her principal research interests are human herpes viruses and childhood viral diseases and vaccines. She is a fellow of the American Academy of Arts and Sciences, the National Academy of Medicine, the American Association for the Advancement of Science, the Infectious Disease Society of America and the American Pediatric Society. She is the recipient of an NIH MERIT award, and has been given honors for basic and translational research, including the University of Pennsylvania School of Medicine Distinguished Graduate Award, the Stanford University School of Medicine Dean's Medal and Albion Walter Hewlett Award, the E. Mead Johnson Award for Research in Pediatrics and the John Enders Award in Virology.

Arvin said she looks forward to having more time for her laboratory research in virology and to ensuring that her successor as vice provost and dean of research has a smooth transition. ISM



L.A. CICERO / STANFORD NEWS SERVICE

Ann Arvin will return to research and teaching after stepping down as the dean of research next fall.

# Initiative aims to help develop innovative companies for brain health

By Tracie White

Brainstorm, an initiative that aims to foster creative and entrepreneurial companies to improve brain health, launched recently with an event featuring a *Shark*

*Tank*-style competition between virtual reality researchers.

"Virtual reality and augmented reality offer exciting potential to transform the way that we as physicians diagnose and

treat diseases like PTSD, autism, anxiety and opioid use," said Nina Vasan, MD, a psychiatry resident and MBA student at Stanford, and founder and director of Brainstorm. "Brainstorm wanted to capture this potential by identifying promising VR/AR applications and working with entrepreneurs to develop their ideas into successful ventures."

Six teams made the finals in October. They included a high school team that presented a virtual reality game which simulates what it's like to have schizophrenia, and a team of researchers from the Medical College of Wisconsin that designed a video game for promoting real-time tools for overcoming anxiety. The teams came from across the country to appear before a panel of judges at the Li Ka Shing Center for Learning and Knowledge. The event was part of Stanford's annual Innovations in Psychiatry and Behavioral Health conference.

The winner of the competition was a

research team from Simon Fraser University in Canada that is investigating the use of neurosensors connected to a virtual reality system designed to help determine what can trigger a relapse in a recovering addict.

Brainstorm, whose interdisciplinary team members hail from across Stanford and the nation, is a special initiative of Laura Roberts, MD, professor and chair of psychiatry and behavioral sciences at Stanford.

The initiative provides courses and educational materials and hosts regular events supporting the growth of entrepreneurial ideas in the field of brain health, Vasan said.

"We wanted to bring the Silicon Valley-style of problem-solving to psychiatry," Vasan said. "Our goal is to bring together pioneering people and create innovative technology and companies that will transform the way brain and behavioral health is addressed." ISM

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# Stanford Medicine Advisory Council charter is revised and formalized

Livingston appointed university liaison for Stanford Medicine

By Kathleen Sullivan

Stanford President Marc Tessier-Lavigne, PhD, has worked with Stanford's biomedical leaders to formalize an advisory council to consult and work with the university and Stanford Medicine on matters of strategic and operational importance affecting the School of Medicine, Stanford Health Care and Lucile Packard Children's Hospital Stanford.

In addition, a new role of university liaison for Stanford Medicine will be filled by Randy Livingston, MBA, vice president of business affairs and chief financial officer at Stanford.

"Although the advisory council has been in existence for a few years, the decision to revise and formalize its charter emerged from conversations with many people, including our clinical faculty chairs and biomedical leaders, about how we could all better engage and more effectively collaborate," Tessier-Lavigne said. "It was also clear that we needed a designated person from the university to be a liaison, to bring new ideas and initiatives to our attention. I'm pleased Randy has agreed to serve in that key role."

The chair of the advisory council is Mariann Byerwalter, MBA, who has a long history of service and commitment to the Stanford community. She has served three terms on the Stanford University Board of Trustees and has served more than two decades on the boards of directors of both hospitals. She chaired the board of directors of Stanford Health Care from 2006 to 2013 and was interim president and CEO of Stanford Health Care in 2016. At the university, she was vice president for business affairs and chief financial officer from 1996 to 2000. Currently, she chairs the board of directors of SRI International.

"I am honored to chair the Stanford Medicine Advisory Council, which was

initially established by President John Hennessy," Byerwalter said. "President Tessier-Lavigne has enhanced the council's charge, formalized its role, and we have worked together to ensure that Stanford Medicine and the university collaborate and execute with greater integration. We look forward to a productive year as we meet challenges and identify opportunities where Stanford is uniquely positioned to lead."

## An 'invaluable role'

Lloyd Minor, MD, dean of the School of Medicine, said he was "extraordinarily pleased" by the evolution of the Stanford Medicine Advisory Council.

"Since its inception, the council has worked tirelessly to support and promote the Principles of Stanford Medicine, which articulate the critical importance of all three aspects of the Stanford Medicine mission: research, teaching and patient care," Minor said. "By formalizing the council and appointing a university liaison, we are shining an even brighter light on our indispensable connection to the whole campus community."

Both hospital leaders concurred that the formalized council will help the medical entities advance and plan together.

"The advisory council will play an invaluable role as we pursue new opportunities to strengthen and integrate each facet of the Stanford Medicine tripartite mission," said David Entwistle, president and CEO of Stanford Health Care. "It will also help enable us to respond effectively to ongoing changes in the health care landscape."

"The revisions to the charter and the appointment of Randy Livingston as liaison will greatly enhance communication and alignment," said Christopher Dawes, president and CEO of Stanford Children's Health.

In September, the 20-member advisory council held its first meeting of the 2017-18 academic year.

The members of the advisory council

include the dean and three department chairs from the School of Medicine; the CEOs, board chairs and members of the board of directors of Stanford Health Care and Lucile Packard Children's Hospital Stanford; current and former members of the Stanford University Board of Trustees; the university liaison for Stanford Medicine; and Stanford's general counsel.

The advisory council will:

- Review and advise on the comprehensive strategic plan for Stanford Medicine that is being developed and conduct periodic reviews of progress relative to the plan.

- Serve as a sounding board to Stanford Medicine leadership and governance on strategic and major operational issues, such as land use, financial planning assumptions and other issues of common interest to Stanford Medicine and Stanford University.

- Coordinate development of, and periodically review and comment on, Stanford Medicine's consolidated capital plan, financial projections and financial performance, including interim integrated review of financial performance on a quarterly basis.

- Conduct ad hoc reviews of specific issues and exceptional matters, such as the status and costs of opening and/or transitioning to the new hospitals.

Livingston will retain his existing roles as vice president of business affairs and chief financial officer while assuming his new role as university liaison for Stanford Medicine.

As university liaison, Livingston is responsible for extending collaboration and ensuring coordination on nonacademic matters between the university

and Stanford Medicine.

"I look forward to working with Lloyd Minor, David Entwistle and Christopher Dawes to enhance the day-to-day working relationship between Stanford Medicine and the university," Livingston said.

"Stanford Medicine is an invaluable university asset, and this new structure will allow us to further inform and educate the entire Stanford community about the incredible biomedical initiatives underway across our campus — many of which involve members of our six other schools beyond medicine."

Livingston has many responsibilities as university liaison, including keeping university leadership informed about the performance, operations, strategy

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Randy Livingston will be responsible for extending collaboration and ensuring coordination on nonacademic matters between the university and Stanford Medicine.

and capital plans for each entity of Stanford Medicine, bringing university concerns to the attention of Stanford Medicine leadership, and serving on the Stanford Medicine Advisory Council and the boards of Stanford Health Care and Lucile Packard Children's Hospital Stanford. ISM

# Multidisciplinary care team prevails against heart defect in newborn

By Erin Digitale

Marlo Greenfield was halfway through her pregnancy when she and her husband, David, received bad news: Their eagerly awaited daughter had a congenital heart defect.

The fetal aorta and left side of the heart were smaller than normal, ultrasound scans indicated. At first, the couple was told the problem might resolve on its own, but over the next several weeks of Marlo's pregnancy, follow-up scans did not show enough catch-up growth. The baby, whose parents planned to name her Kennedy, would need heart surgery in her first few days of life to ensure she could get enough oxygen.

"It was very scary information to hear when we were hoping for a healthy baby," David said. When Marlo was 32 weeks pregnant, she was referred to the Johnson Center for Pregnancy and Newborn Services at Lucile Packard Children's Hospital Stanford, which helped the couple feel more confident about what was coming.

## Assessing heart with echocardiogram

"Knowing we would be at one of the best hospitals in the nation, with doctors and nurses that strictly deal with children and pregnant women, was reassuring," David said.

Physicians in the hospital's Fetal and Pregnancy Health Program assessed Kennedy's heart with a detailed fetal echocardiogram. They recommended that the family move to Palo Alto from their home in Oakley, California, a few weeks before Marlo's due date so that Kennedy could be born at Packard Children's.



Kennedy Greenfield was treated for a heart defect at Lucile Packard Children's Hospital Stanford.

On July 24, soon after the move, Marlo's water broke. Kennedy arrived a few hours later, and several Packard Children's neonatologists and cardiologists immediately began working to stabilize her.

Kennedy was started on medication that would help maintain her circulation until surgery. Her caregivers in the neonatal intensive care unit, led by neonatologist William Rhine, MD, professor of pediatrics at the School of Medicine, watched her closely.

"There's a certain amount of stabilization that occurs in the first few days of life," Rhine said. "The blood pressure in the baby's lungs drops; you want that to occur before you do cardiac surgery. We also evaluate other organ systems, such as the brain and kidneys, to make sure they are ready for surgery."

From the start, Kennedy was also being monitored by a cardiac intensivist, a pediatric cardiologist who specializes in cardiac care in the intensive care unit. The close collaboration between doctors from different specialties is a hallmark of the top-notch care Packard Children's offers to children born with congenital

heart defects. "Whether a baby is in the NICU or the CVICU, they're going to see both a neonatologist and a cardiac intensivist every day," Rhine said, referring to the neonatal ICU and the cardiovascular ICU. "We think it represents the highest standard of care."

## Ready for surgery

On July 31, at 7 days old, Kennedy was ready for surgery. In a five-hour procedure, Katsuhide Maeda, MD, clinical associate professor of cardiothoracic surgery, and his team put Kennedy on a heart-lung bypass machine and carefully removed the too-small portion of her aortic arch. Once the abnormally narrow region of blood vessel was gone, Maeda reconstructed an aortic arch from the infant's own blood vessel tissue. "This is a relatively straightforward procedure for our team," Maeda said.

Kennedy did well, staying for four days in the CVICU and then transferring back to the NICU. Her multidisciplinary care team followed her the whole time.

"Every time we spoke to someone, they knew exactly what was going on with Kennedy," Marlo said. "Every single person was on the same page. They really knew what they were doing and had it under control."

The coordination will continue after the cardiovascular intensive care unit relocates to the new main building of Packard Children's when it opens in December. The NICU will stay in the hospital's west building, and will eventually expand as existing hospital spaces are renovated and repurposed into a world-class mother and baby center over the next few years.

In the meantime, Kennedy has been home with her family in Oakley since August.

"She's absolutely beautiful, very content and happy," David said. "Of course, I'm a little biased, but I think she's perfect in every way." ISM

# Clinical trial finds blood-plasma infusions for Alzheimer's safe, promising

By Bruce Goldman

School of Medicine investigators have reported success in an early-phase clinical trial examining the safety, tolerability and feasibility of administering infusions of blood plasma from young donors to participants with mild to moderate Alzheimer's disease. There were also some signs suggesting improvements in participants' conditions.

Results from the PLASMA trial, short for Plasma for Alzheimer's Symptom Amelioration, were presented Nov. 4 at the 10th annual Clinical Trial on Alzheimer's Disease conference in Boston by Sharon Sha, MD, a clinical associate professor of neurology and neurological sciences at Stanford and the trial's principal investigator.

Sha noted that the finding of safety wasn't surprising, given that blood-plasma infusions have long been in widespread use for other indications and are considered extremely safe. More surprising, she said, were hints of recipients' improvement on tests of functional ability: the capacity to perform basic tasks essential to independent daily life, such as remembering to take medications and being able to pay bills and prepare one's own meals.

The PLASMA trial was designed to test a hypothesis advanced by Tony Wyss-Coray, PhD, Stanford professor of neurology and neurological sciences and

a senior research career scientist at the Veterans Affairs Palo Alto Health Care System, whose research has shown that factors in the blood of young mice can rejuvenate the brain tissue and improve cognitive performance in old mice.

## Larger studies needed

Sha, the clinical core co-leader of the Stanford Alzheimer's Disease Research Center and the medical director of the Stanford Neuroscience Clinical Trials Group, cautioned that these assessments were based on caregiver reports and that the number of participants in the study — 18 — was small. Further studies on larger numbers of participants will be necessary before conclusions about efficacy can be reached, Sha said.

The trial took place at Stanford Hospital and was sponsored by Alkahest, a privately held biotechnology company headquartered in San Carlos, California. Alkahest holds intellectual property associated with the treatment regimen. Wyss-Coray, a co-founder of the company and chair of its scientific advisory board, continues to work full-time at Stanford. He was not involved in the clinical study.

The trial proceeded in two stages. In the first stage, nine participants with mild to moderate Alzheimer's disease were given four weekly infusions either of plasma — the liquid, cell-free part of blood — obtained from donors 18-30 years old, or of placebo (a saline solu-

tion). Neither the participants nor those administering the infusions knew which of the two infusions any given participant was getting. Then, after a six-week "washout" period, the regimens were reversed: Those initially receiving plasma got four weekly infusions of placebo, and vice versa.

"Those participants served as their own controls," said Sha.

Multiple tests and questionnaires to

ascertain mood, cognition and functional ability of the participants were administered to either participants or their caregivers before and after the first four-week infusion period, and again before and after the second four-week infusion period.

The total time elapsing between a participant's first and final visits, including a preliminary screening and a final visit, approached six months. The participants needed to make nearly a dozen round trips to Stanford, accompanied by their caregivers. So, to reduce the travel burden, the investigators decided to modify the design for their next group of nine participants. These newcomers all received young-donor plasma infusions, and they and their caregivers, as well as the administrators, all knew it. This change cut the time between the first and final visits to 10-12 weeks for the second group of participants, and required commensurately fewer trips. These participants, like the first group, received the full battery of mood, cognition and functional-ability assessments.

Only a single instance of a trial-related adverse event — excessive itching — occurred. Sha said this wasn't entirely unanticipated, as it can arise as a side effect of the infusion of any blood product. Another participant had a stroke, but this was considered unrelated to the treatment; the participant had received only four infu- **See PLASMA, page 5**



PAUL SAKUMA

Sharon Sha led a safety trial in which participants with Alzheimer's receiving blood plasma from young donors showed some evidence of improvement.

# New study finds drawbacks to robot-assisted kidney removal

By Krista Conger

Robot-assisted laparoscopic surgery to remove a patient's entire kidney requires slightly longer operating times and results in increased costs compared with the use of traditional laparoscopic surgery, according to a large, multiyear analysis conducted by researchers at the School of Medicine.

However, the two approaches have comparable patient outcomes and lengths of hospital stay, the study showed. Laparoscopic surgery is a minimally invasive procedure in which surgical operations are done through small incisions. The removal of the entire kidney is called a radical nephrectomy.

"Although the laparoscopic procedure has been standard of care for a radical nephrectomy for many years, we saw an increase in the use of robotic-assisted approaches, and by 2015 these had surpassed the number of conventional laparoscopic procedures," said Benjamin Chung, MD, associate professor of urology. "We found that, although there was no statistical difference in outcome or length of hospital stay, the robotic-assisted surgeries cost more and had a higher probability of prolonged operative time."

The discrepancy may be due to the time needed for robotic operating room setup or due to a surgeon being in the earlier part of his or her learning curve, resulting

in a subsequent increase in operating room and instrumentation costs, the researchers speculated.

Chung is the senior author of the study, which was published Oct. 24 in *JAMA*. The lead author is former Stanford visiting scholar In Gab Jeong, MD, PhD.

## The dexterity of robots

Surgical robots are helpful because they offer more dexterity than traditional laparoscopic instrumentation and use a three-dimensional, high-resolution camera to visualize and magnify the operating field. Some procedures, such as the removal of the prostate or the removal of just a portion of the kidney, require a high degree of delicate maneuvering and extensive internal suturing that render the robot's assistance invaluable. But Chung and his colleagues wondered whether less technically challenging surgeries, such as the removal of a whole kidney, may not benefit as significantly from a robot's help.

The researchers analyzed data from 416 hospitals across the country from 2003 to 2015. They found that in 2003 about 65 percent of patients with kidney tumors that necessitated the removal of the entire organ underwent an open surgical procedure. About 34 percent had their kidney removed using a laparoscopic procedure, and only the remaining 1.5 percent of cases were conducted with robot-assisted surgery. By 2015, the proportion of patients who underwent the open procedure had decreased to about 50 percent, but the use of robot-assisted laparoscopic surgery for the remaining cases had surpassed that of traditional laparoscopic surgery, 27 percent to 23 percent.

When they pooled the data across the years, the researchers found that among nearly 24,000 patients, almost 19,000 underwent a traditional laparoscopic procedure and about 5,000 underwent a robotic-assisted procedure. They found that 46.3 percent of those

patients whose surgeon used the robot had a total procedure time of more than four hours. In contrast, about 28.5 percent of the patients whose surgeon used the conventional laparoscopic procedure were in the operating room for more than four hours.

On average, the total hospital cost (including the cost of supplies, room and board, pharmaceuticals and operating room time) for the robot-assisted procedure exceeded that of the traditional laparoscopic procedures by about \$2,700 per patient. The researchers speculated that the increased cost may be due to longer times spent in the operating room and the disposable instruments upon which surgical robots rely.

## Why use robotic assistance?

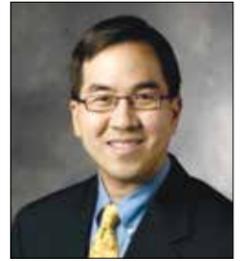
The increase in robot-assisted surgery for many procedures may be due to a variety of factors, the researchers said. The technology clearly benefits patients for certain types of surgeries. In other situations, there may be an expectation on the part of the hospital or the surgeons themselves to justify the large initial investment in purchasing the robot by using it for many types of procedures. And, regardless of the procedure, use of the robotic platform can assist the surgeon in many ways to make the operation more comfortable for the surgeon. Finally, patients themselves may view robot-assisted surgery as more technologically advanced.

Chung noted that the study covers a time period when many physicians were just learning to use the robots for this type of procedure; as time passes, it's possible the operating time will decrease and that the cost differences between the two procedures will narrow. But for now, the study suggests that robot-assisted surgery isn't always the right choice.

"There is a certain incentive to use very expensive equipment," said Chung. "But it is also important to be cognizant as to how our health care dollars are being spent. Although robotic surgery has some advantages, are those advantages relevant enough in this type of case to justify an increase in cost?"

Other Stanford authors of the study are former research scholar Yash Khandwala; and former visiting scholars Jae Heon Kim, MD, PhD, and Deok Hyun Han, MD, PhD.

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



Benjamin Chung



MASTER VIDEO / SHUTTERSTOCK.COM

Robot-assisted surgeries for kidney removal have been on average less cost-effective and more lengthy than traditional laparoscopic nephrectomies, according to a new study.

# Technology invented by researchers ties brain circuits to alertness

By Bruce Goldman

Stanford investigators have for the first time tied several brain circuits to alertness.

The findings enhance scientists' understanding of the forces driving alertness, a brain state that's essential to survival, by showing that diverse cell types throughout the brain together produce this state.

Problems tied to alertness deficits range from sleep deprivation to depression to brain-trauma-induced somnolence, while conditions such as anxiety, mania and post-traumatic stress disorder are often characterized by excessive alertness.

The researchers employed a cutting-edge technology that allowed them to monitor vast numbers of nerve cells' activity in the brain simultaneously and, afterward, to characterize the cells of interest in molecular detail. This new method lets scientists record the activity of any cell type, without needing to produce special, genetically modified animals for each new experiment.

In a study published online Nov. 2 in *Cell*, Karl Deisseroth, a Howard Hughes Medical Institute Investigator and professor of bioengineering and of psychiatry and behavioral sciences at Stanford, and his colleagues describe how they managed to observe activity in nearly every nerve cell, or neuron, in the brains of larval zebrafish while tracking the creatures' reaction times in response to a stimulus. (Studies in humans and other animals have shown that reaction times are faster when the subject is more alert). The activity of each neuron was then linked to that neuron's particular cell type. With this brainwide dragnet, Deisseroth and his associates were able to determine the identities of several distinct neuronal circuits not previously suspected to be associated with alertness.

The study's lead author is postdoctoral scholar Matthew Lovett-Barron, PhD.

## Extending findings to mice

It turns out that alertness involves more than a single on/off switch. Prior to the new study, alertness in vertebrates was thought to be primarily controlled by a set of neurons emanating from a brain structure called the locus coeruleus

and radiating to regions throughout the brain.

Importantly, the researchers extended their findings to mice, confirming that the same circuits tied to alertness in zebrafish are acting similarly in mammals, whose ancestors split from those of zebrafish hundreds of millions of years ago. "This tight conservation of alertness-promoting circuits over such long epochs of evolutionary time — longer than human and mouse lineages have been separated — strongly implies relevance to humans as well," said Deisseroth, who holds the D.H. Chen Professorship.

The Stanford scientists call the new method they developed MultiMAP, which is short for Multiplexed-alignment of Molecular and Activity Phenotypes. It let them track the activity of nearly every neuron in the zebrafish brain and then identify the cell type of every neuron of interest — the crucial step in determining which neuronal circuits are participating in the induction of a brain state such as alertness.

"We looked at every neuron in the fish's brain during life, when those cells were actively firing, and learned which cells were most active at moments when we knew that the fish was most alert," said Deisseroth. "Then, after the fish's brain tissue was preserved with a fixative without altering relative positions of cells within the fish's head, we could target those neurons with molecular probes and determine their cell types."

In particular, the investigators wanted to explore the activity of the brain's neuromodulatory circuitry. Distinct from their more binary cousins — some 98 percent of neurons in the brain act by either exciting or inhibiting downstream nerve cells — clusters of neuromodulatory neurons send out projections that branch throughout the brain and act less like on/off switches than like colors on an artist's palette. Rather than excite or inhibit, they instead add nuance by secreting substances that render excitatory and inhibitory neurons more or less likely to fire under various circumstances.

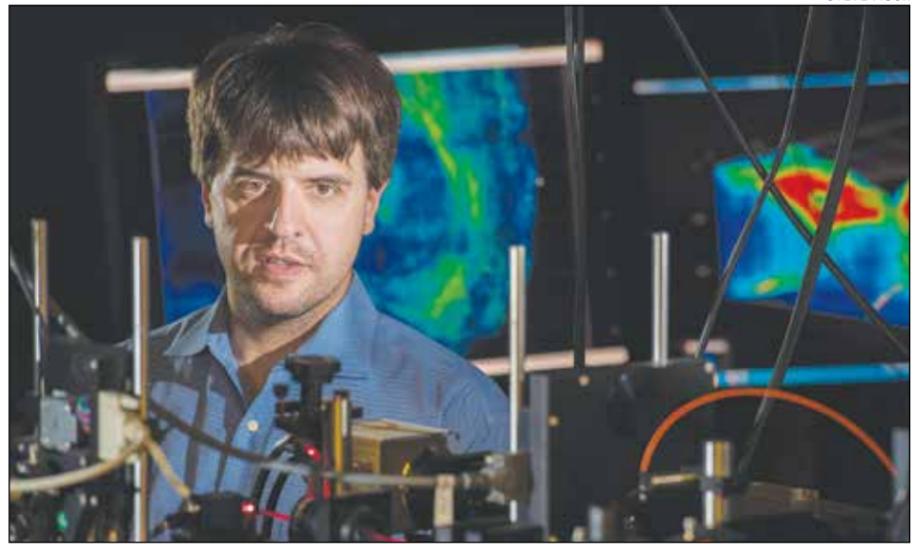
Different types of neuromodulatory neurons can be distinguished not only by the different kinds of substances they secrete, such as dopamine, acetylcholine and serotonin, but also by various biological markers, such as proteins that

the investigators themselves knew they were getting plasma; this could perhaps predispose caregivers to optimistic reporting. But examination of the data indicated that, to the contrary, it was the first group of participants — who had no idea whether they were getting plasma or placebo — who showed the most improvement in functional ability after receiving plasma infusions.

"Our enthusiasm concerning these findings needs to be tempered by the fact that this was a small trial," Sha said. "But these results certainly warrant further study."

Alkahest has stated in a news release that based on the safety profile and signals of efficacy seen in the PLASMA trial, it is planning to advance the clinical development of a next-generation, proprietary plasma-derived product for the treatment of mild to moderate Alzheimer's disease.

"I'm excited to see that giving repeated infusions of plasma to elderly people with Alzheimer's disease is safe and that we can move forward to larger studies," Wyss-Coray said. "But I'm also realistic enough to know that it is very easy to cure diseases in small animals and a million times more difficult in humans." ISM



Karl Deisseroth and his colleagues were able to simultaneously monitor activity in every nerve cell of a zebrafish's brain and determine which types of neurons were tied to alertness.

appear in or on one but not another neuromodulatory cell type.

The zebrafish Deisseroth's group looked at were only 7-10 days old — a time when their bodies are only a few millimeters in length and still relatively transparent, yet are able to execute complex behavior. This feature, along with a few tricks the scientists cooked up, permitted direct brain-wide optical inspection of neural activity.

## Bioengineered fish

The fish had been bioengineered so that calcium flux within a neuron — an excellent proxy for impulse conduction within that cell — triggered a fluorescent signal that could be picked up and recorded via high-powered microscopy. The researchers constrained the fish's heads by embedding each tiny animal in an agarose gel. They carved the gel away from the fish's tail, whose movements would be key to their experiments.

To test alertness, the investigators presented the fish with a visual stimulus suggestive of an approaching predator. This evokes an instinctive tail-swishing response, as the fish attempts to veer away from impending danger. Each of 34 separate larval zebrafish was subjected to repeated exposures to the looming-predator stimulus. The time elapsed between each exposure and the consequent swishing of the fish's tail — the animal's reaction time — was measured. In each instance, fluorescence representing activity within tens of thousands of nerve cells just prior to the stimulus was captured and recorded.

After humane euthanasia and preserving the fish tissue in fixative, the team directed fluorescence-labeled molecular probes at the animals' neurons and imaged the results. Using algorithms, they were able to align the neural-activity data from their experiments on live zebrafish with cell-identity data extracted afterward from those same fish.

Deisseroth and his colleagues identified multiple anatomically and biochemically distinct populations of neurons that were most active just before the fishes' fastest responses to the looming-predator stimulus. One of these was the norepinephrine-secreting population originating in the locus coeruleus, already well-known to be involved in alertness. This was reassuring, Deisseroth said, because it indicated that the approach was valid.

But the dragnet snagged several other neuromodulatory populations of neurons as well, including cells that release acetylcholine, serotonin, dopamine and the peptides CART, somatostatin and neuropeptide-Y. While all these populations' activity levels correlated with alertness, they didn't correlate in perfect lockstep with one another, suggesting that each population has its own slightly different job to do.

Guided by their findings in zebrafish, the researchers then targeted the equivalent neuronal populations in the much more complex brains of mice. To test mice's reaction times, they trained the mice to lick in response to a particular tonal cue; when the mice did so, they were rewarded with a drop of drinking water.

Deisseroth's team observed almost precisely the same activity patterns in these equivalent circuits in mice that they had seen in those of the fish.

The scientists went one step further in the mice: They used optogenetics — a technology, developed in Deisseroth's lab, that allows neurons to be excited or inhibited by a pulse of light at the flick of a switch — to prove, by variously activating or inhibiting neurons in one or another population, that only a subset of the circuits in question were individually capable of increasing alertness. One was the set of neurons coming from the locus coeruleus; this set operates by secreting the substance norepinephrine. Another was an understudied group of so-called CART neurons, previously known to be responsive to cocaine and amphetamines, in a brain region called the Edinger-Westphal nucleus; and the third was a group of acetylcholine-secreting neurons in a deep-brain structure called the lateral dorsal tegmentum. Other cell types correlated with alertness did not directly influence the behavior; Deisseroth said he thinks these neuromodulatory circuits, rather than directly triggering alertness, report on its status to other brain circuits.

The new findings open the door to a whole new route of further exploration, Deisseroth said. "The more we understand the landscape of neurons that underlie a brain state like alertness, the more we understand the brain state concept itself — and we may even be able to help design brain-state targeted clinical interventions."

Other Stanford co-authors are basic life research scientist Aaron Andalman, PhD; graduate students William Allen, Sam Vesuna and Isaac Kauvar; and former graduate student Vanessa Burns, PhD.

The study was funded by the Helen Hay Whitney Foundation, the Brain and Behavior Research Foundation, the National Institute of Mental Health, the National Institute on Drug Abuse, the Defense Advanced Research Projects Agency NeuroFAST program, the Howard Hughes Medical Institute, the NOMIS Foundation, the Else Kroner Fresenius Foundation, the Wiegers Family Fund, the James Grosfeld Foundation, the HL Snyder Foundation and the National Science Foundation.

Stanford's departments of Bioengineering and of Psychiatry and Behavioral Sciences also supported the work. The Department of Bioengineering is jointly operated by the School of Medicine and the School of Engineering. ISM

## Plasma

continued from page 4

sions of saline and, furthermore, had suffered the stroke at the end of the ensuing washout period, during which no infusions of any kind were administered.

## Improvements in functional ability

An analysis of assessments once all participants had been treated showed no significant changes in participants' mood or their performance on tests of cognition involving tasks such as memorizing lists or recalling recent events, Sha said. These kinds of changes are typically observed only in clinical trials whose durations exceed one year, she added, so the absence of an effect here wasn't particularly unanticipated.

But on two of three different assessments of functional ability, participants showed statistically significant improvement — this, despite the trial's small size.

"That was surprising, to me," said Sha. "The trial wasn't powered to show efficacy."

At first, the investigators suspected that the report of improvements in functional ability might have been driven by the second group of participants, who along with their caregivers and

# Marijuana

continued from page 1

“Frequent marijuana use doesn’t seem to impair sexual motivation or performance. If anything, it’s associated with increased coital frequency,” said the study’s senior author, Michael Eisenberg, MD, assistant professor of urology. The lead author is Andrew Sun, MD, a resident in urology.

## Hint of a causal connection

The study does not establish a causal connection between marijuana use and sexual activity, Eisenberg noted. But the results hint at it, he added. “The overall trend we saw applied to people of both sexes and all races, ages, education levels, income groups and religions, every health status, whether they were married or single and whether or not they had kids.”

The study is the first to examine the relationship between marijuana use and frequency of sexual intercourse at the population level in the United States.

“Marijuana use is very common, but its large-scale use and association with sexual frequency hasn’t been studied much in a scientific way,” Eisenberg said.

According to the National Institute on Drug Abuse, more than 20 million adult Americans are current marijuana users. With the drug’s legalization for medical or recreational use in 29 states, that number is climbing. But despite marijuana’s growing status as a recreational drug, its status as a procreational drug remains ambiguous: On one hand, there are reports of erectile dysfunction in heavy users, and rigorous studies have found reduced sperm counts in men

who smoke it; on the other hand, experiments conducted in animal models and humans indicate that marijuana stimulates activity in brain regions involved in sexual arousal and activity.

## Looking at survey responses

To arrive at an accurate determination of marijuana’s effect on intercourse frequency, Eisenberg and Sun turned to the National Survey of Family Growth, sponsored by the federal Centers for Disease Control and Prevention. The survey, which provides data pertaining to family structures, sexual practices and child-bearing, reflects the overall demographic features of the U.S. population. Originally conducted at regular intervals, the survey is now carried out on an annual basis. It explicitly queries respondents on how many times they’ve had intercourse with a member of the opposite sex in the past four weeks, and how frequently they’ve smoked marijuana over the past 12 months.

The investigators compiled answers to those questions for all years since 2002, when the survey first began collecting data on men as well as women. They included data from respondents ages 25–45 and excluded a small percentage (fewer than 3 percent) of respondents who had failed to answer one or more relevant questions.

In all, Eisenberg and Sun obtained data on 28,176 women averaging 29.9 years of age and 22,943 men, whose average age was 29.5. They assessed these individuals’ self-reported patterns of marijuana use over the previous year and their self-reported frequency of heterosexual intercourse over the previous four



STEVE FISCH

Michael Eisenberg is the senior author of a study that is the first to examine the relationship between marijuana use and frequency of sexual intercourse at the population level in the United States.

weeks.

Some 24.5 percent of men and 14.5 percent of women in the analysis reported having used marijuana, and there was a positive association between the frequency of marijuana use and the frequency of sexual intercourse. This relationship applied to both sexes: Women denying marijuana use in the past year, for example, had sex on average 6.0 times during the previous four weeks, whereas that number was 7.1 for daily pot users. Among men, the corresponding figure was 5.6 for nonusers and 6.9 for daily users.

In other words, pot users are having about 20 percent more sex than pot abstainers, Eisenberg noted.

## Positive association is universal

Moreover, Eisenberg said, the positive association between marijuana use and coital frequency was independent of

demographic, health, marital or parental status.

In addition, the trend remained even after accounting for subjects’ use of other drugs, such as cocaine or alcohol. This, Eisenberg said, suggests that marijuana’s positive correlation with sexual activity doesn’t merely reflect some general tendency of less-inhibited types, who may be more inclined to use drugs, to also be more likely to have sex. In addition, coital frequency rose steadily with increasing marijuana use, a dose-dependent relationship supporting a possible active role for marijuana in fostering sexual activity.

Nevertheless, Eisenberg cautioned, the study shouldn’t be misinterpreted as having proven a causal link. “It doesn’t say if you smoke more marijuana, you’ll have more sex,” he said.

Stanford’s Department of Urology supported the work. **ISM**

# Medicine

continued from page 1

people from underrepresented groups, he said. That compares with 12 percent of PhD students and 14 percent of medical students in 2012.

“So it’s really wonderful to see the time and effort and devotion really coming to benefit in terms of the students we’re attracting,” Minor said. “We’re building an affirming community that is inclusive and representative of everyone.”

a high level of sustainability, extensive open spaces, a sanctuary for spiritual reflection and technologies to put children at ease while they undergo challenging procedures, he said.

Soft floors, wood paneling in rooms, ubiquitous flower boxes, children’s play areas and many other amenities are designed to make the hospital as child- and family-friendly as possible, he said.

“We wanted to create a place that not only would cure disease but also a facility that would be nurturing and would feel comfortable to young children and their

tients and their infants, he said.

David Entwistle, president and CEO of Stanford Health Care, highlighted Stanford Medicine’s integrated strategic plan, in which the two hospitals and the medical school are working in concert to determine their future direction and how best to get there.

## Planning the future

Stanford Medicine has been seeking feedback from faculty and staff and received 3,700 responses so far. Thirteen working groups have been created to focus on specific areas, such as digital health, precision health and translational medicine, he said. The collaborative effort is an example of how the three organizations are breaking down barriers and trying to overcome what has been a siloed culture, he said.

“Quite frankly, that is what will lead to our success — that ability to work together and collaborate,” Entwistle said.

In response to a question about proposed cuts in health care funding, Entwistle said the hospital has been aggressively fighting back against proposed federal legislation that could be “quite frankly catastrophic.” For instance, the recent Graham-Cassidy health bill, which failed to gain sufficient support in the Senate, would have cut \$275 billion from Medicaid, including \$95 million in California, where the program is known as Medi-Cal, he said.

At Packard, the impact of the proposed funding cuts could have been dire, Dawes said. He said 50 percent of children born in California depend on Medi-Cal, and 42 percent of Packard’s patients rely on the federally funded program. A decline in these funds, he said, could have had a “profound” impact on the hospital and the families it serves.

“Our first initiative is to try to prevent these changes from happening,” said Dawes. “We need to continue to fighting aggressively any changes to Medicaid and at the same time prepare ourselves to be more cost-efficient.”

Given today’s unpredictable political environment, Minor said it’s more important than ever to build a strong community at Stanford Medicine.

“In these times of enormous uncertainty in our country, it’s important that we do what we can to build our community and affirm in our actions the value we have for each other,” he said. “I think that’s really, really important to enable us to be successful internally but also to show the world what a cohesive, highly functioning community can do.” **ISM**



ROD SEARCEY

Christopher Dawes discussed some of the features of the expanded Lucile Packard Children’s Hospital Stanford that will open in December.

Chris Dawes, president and CEO of Stanford Children’s Health, discussed the new children’s hospital, which is tentatively scheduled to open Dec. 9. The new facility, driven by the vision of the late Lucile Packard and her daughter, Susan Packard Orr, incorporates

families,” he said. “We wanted to make sure we had a facility that was not ‘institutional.’”

The current hospital, which will be called the West Building, ultimately will be revamped as a mother and baby center, with private rooms serving obstetric pa-

## 5 QUESTIONS

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

# Margo Thienemann on guidelines for treating an alarming psychiatric disease in children

For the last five years, a group of clinicians at the Stanford School of Medicine and at Lucile Packard Children's Hospital Stanford have focused on what happens when the immune system attacks a child's brain.

In Pediatric Acute-Onset Neuropsychiatric Syndrome, which is believed to stem from brain inflammation after a triggering infection, children suddenly develop severe obsessive-compulsive symptoms and other behavioral problems. They urgently need medical and psychiatric help. Yet many pediatricians and mental health professionals still lack awareness of how to treat the disorder.

To fill the gap, a multidisciplinary team of experts from several universities has pub-

lished the first set of peer-reviewed treatment guidelines for PANS and its companion diagnosis, Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections, or PANDAS. Margo Thienemann, MD, clinical professor of psychiatry and behavioral sciences at Stanford, is the lead author of the portion of the guidelines that address psychiatric and behavioral interventions. Thienemann co-directs Packard Children's PANS clinic, the first in the country exclusively devoted to the disease, with Jennifer Frankovich, MD, clinical associate professor of pediatric rheumatology.

Thienemann spoke with Erin Digitale about why the guidelines were needed and what else can be done to raise awareness of the condition.

### 1 What do children and families affected by PANS/PANDAS experience?

**THIENEMANN:** Parents often describe children as turning into somebody completely different overnight. A child who was functioning just fine might suddenly feel like they had been "possessed" by something. They may be tearful and unable to separate from their parents. They may suddenly develop vocal or motor tics. The child may suddenly, after never having had appreciable obsessive-compulsive symptoms, engage in long periods of checking behaviors or cleaning behaviors, over and over. It suddenly takes hours to get out of the house or get the child to bed.

In addition to OCD symptoms, the other cardinal symptom is food refusal. Kids will suddenly be afraid to eat for fear they will choke, or fear that the food is poisoned, contaminated or spoiled. They may say food smells awful or express fear of vomiting. Again, this appears out of nowhere.

It's like being hit by a train. Most often, the child will miss some school and at least one parent has to take a leave from work. It's extremely anxiety-provoking because a normally functioning child suddenly can't go to school, sleep, eat or be apart from parents, and is involved in rituals and tics. Another thing that's very disruptive is trying to find someone who will provide medical and psychiatric care for your child. How do you find someone if providers say "I don't believe in it" or "I don't know how to treat this"?

### 2 Why were the PANS/PANDAS treatment guidelines needed?

**THIENEMANN:** Right now, there isn't enough solid, empirical evidence to say definitively "this is what you do" for these patients. For some aspects of treatment we have evidence, but overall we have to bridge the gap between our current clinical experience and knowledge, and the clinical studies. We are continuing to collect evidence, but many children will be identified with PANS/PANDAS before that work is complete. Physicians and other professionals need to know what to do for them now.

Also, despite the fact that we published diagnostic guidelines for PANS/PANDAS in 2015, I think some physicians still feel it's not legit. We want physicians to take this disease seriously and, even more importantly,

we really want them to treat it.

### 3 What are some of the most important elements of the guidelines?

**THIENEMANN:** The treatment is at least tri-part. The main thrust of treatment is that if there is a triggering infection, we should treat the infection, and also treat close contacts who may be exposing the child to infection. We also have to treat inflammation, which is what we think causes the brain symptoms.

The psychiatric portion of the guidelines recognizes that the child and family are really suffering and the child needs psychiatric treatment to help with symptoms. We have to manage the child's distress so they can get medical treatment, get blood drawn, get MRIs, take medications, so the family can sleep, and the child can sleep. We also need to help the family understand what might be going on, what they can anticipate from treatment, how to interact with each other and their child around the illness, and how to interact with the child's school.

Unfortunately, a lot of the tools in psychiatry are medications — for OCD, depression, ADHD, tics — that don't work the same way on an acutely inflamed nervous system as they would on garden-variety, idiopathic childhood mental illnesses. When medications are used, usually for residual symptoms, the guidelines suggest beginning with one-fourth of the typical starting dose of medication and increasing the dose very slowly. There can be complex interactions between medications, and between the medications and other changing variables related to where a child is in the illness and concomitant treatments. It makes treatment complicated.

### 4 What are some of the gaps in how our health care system is set up to treat these children?

**THIENEMANN:** Unfortunately, we lack a good place to hospitalize these kids.

If we put them in a pediatric hospital when they're unpredictably agitated or rageful, it doesn't work. Pediatric hospitals are not set up for kids who may run

out of the hospital or hit someone. Little sounds bother PANS/PANDAS patients, so the constant beeping of monitors doesn't help, and lights bother them, so they don't sleep in a hospital setting. It can be very difficult on hospital staff.

Psychiatric hospitals are also hard for these patients to tolerate. They have a brain inflammation problem, not a behavioral problem, so typical behavioral interventions aren't helpful. And in psychiatric settings, parents don't get to stay with their children. For many other pediatric psychiatric diagnoses, the parents may be a part of the problem, and some of the process of diagnosis is seeing how the child acts away from parents. But most children with PANS/PANDAS have terrible separation anxiety as part of their illness, and it's very hard on them to be away from their parents. Psychiatric hospitals also are usually not comfortable working up an infection

or giving intravenous treatment, which is required for some of the immune therapies used for this disease, so the children's medical needs can't always be met in a psychiatric setting.

Often, there is no place other than home to treat children with PANS/PANDAS, which can be really hard on the family. Ideally, for the future, I see a day when we have med-psych units for these patients in the same way that we now have excellent med-psych units for eating disorders. We would need hospital staff who specialize in addressing the psychiatric problems and family stress that go along with PANS/PANDAS, as well as people who can diagnose and treat the more traditional medical problems.

### 5 What other changes do we need next for PANS/PANDAS patients?

**THIENEMANN:** Early identification. When someone comes to their doctor with sudden behavioral change, emotional change, suddenly has tics or suddenly stops eating, this disease should automatically be on the differential diagnosis. If we identify it early, it's less complicated to treat and the patients have better outcomes.

ISM



Margo Thienemann

## Baseline

continued from page 1

able participant in the longitudinal study; as a breast cancer survivor and a woman, her biological data could provide important information for researchers seeking to understand the murky border between health and disease.

The study is the first initiative of Project Baseline, which is a broader effort to establish a well-defined baseline of human health, as well as a rich data platform that may be used to better understand the transition from health to disease. Recruitment at Stanford began in June and is ongoing.

### Wide range of participants needed

"It's important that we enroll a broad spectrum of participants, from those who are healthy to those who have a higher-than-normal risk for cancer or cardiovascular disease," said professor and chair of radiology Sanjiv Sam Gambhir, MD, PhD, the study's principal investigator at Stanford. "We also need people of all ages and ethnic backgrounds. The reason that this is so important is that we want to capture the transition from health to illness at a molecular level. Enrolling people at higher risk can increase the probability that we will observe study participants transitioning to

an ill state during the course of the study. And this transition may look different in different ethnic groups or genders."

Like Purchase, participant Camilo Barcenas, 39, is eager to contribute his health data to the landmark study. "This is a unique time in history," said Barcenas, a health care technology entrepreneur who identifies as Hispanic and has two young children. "We have the capability to collect lots of information about individuals and to analyze that data in a quantitative way to learn even more about ourselves as a species and to use that knowledge for the betterment of humanity."

Participation in the study involves a two-day visit to Stanford, during which participants' health histories and vital signs are assessed and biospecimens such as saliva and blood are collected. Clinical tests such as echocardiograms, CT scans and chest X-rays are conducted, and participants are given an investigational study watch and a sleep sensor to measure their activity levels and sleep patterns. After the initial visit, participants respond to regular surveys via a smartphone, computer or call center, and return to Stanford at least once a year for further data collection.

**"It's important that we enroll a broad spectrum of participants."**



Sanjiv Sam Gambhir

All Project Baseline study data will be hosted on the Google Cloud Platform, with great consideration for data safety, privacy and security. In the future, de-identified data will be made available to qualified researchers for exploratory analysis such as characterizing the variation of the participants and identifying biomarkers of disease-related transitions.

"This study is highly unique in the depth of information it gathers about individuals over time," said Gambhir, who is also the director of the Canary Center for Cancer Early Detection at Stanford. "We want to encourage anyone interested — particularly under-represented minorities, the elderly and those at high risk for cancer or cardiovascular disease — to visit the website to learn more about the study and apply to participate."

"Once you truly understand what the study is attempting to accomplish," said Purchase, "it almost feels like a moral obligation to participate. My youngest daughter is a brain cancer survivor and a huge motivating factor for me. Between my breast cancer and her brain cancer, we are desperate to move medical knowledge forward."

People interested in participating in the study should visit [www.projectbaseline.com](http://www.projectbaseline.com) or call 855-5-BASELINE (855) 522-7354. ISM

# BioSci Careers expands programs to prepare trainees for range of jobs

By Tracie White

BioSci Careers, formerly known as the School of Medicine Career Center, is marking its 15th anniversary by expanding its services to meet the evolving needs of students and postdoctoral scholars.

BioSci Careers, which describes itself as a “career community,” has added new courses in law, public policy, consulting, business, finance and communication as part of an effort to help trainees learn how they can transfer their skills to other professions, said Stephanie Eberle, assistant dean of BioSci Careers.

“It’s not easy for our trainees to make the transition from school to careers,” Eberle said. “Often, they don’t know how to market themselves. They’ve been so focused on one particular facet of science.”

The changes at the career center were spurred in part by studies showing that biosciences graduates are increasingly taking nonacademic jobs. A recent study by the National Institutes of Health showed that almost 80 percent of research-trained professionals in biomedicine nationwide are employed outside academia. At Stanford, those numbers aren’t quite so dramatic, but they’re trending in that direction, Eberle said.

## Alumni survey results

A survey of Stanford alumni with PhDs in the biosciences found that a majority are pursuing careers outside academia, a major shift over that past decade, Eberle said.

The survey examined career trends for biosciences alumni between 2010 and 2015 and found that 52 per-

cent of all respondents were pursuing nonacademic careers. About 30 percent were working in biotechnology. Other areas of work included government, consulting and finance.

BioSci Careers assists more than 2,000 trainees per year in identifying and preparing for future careers in academia, health care, biotechnology, entrepreneurship, data science, education, nonprofit organizations, government, law, finance, government policy and science communication, Eberle said.

“We’re here to help trainees make good career decisions based on fact and self-awareness rather than assumptions and fears,” Eberle said. “Our goal is to help trainees develop their many transferrable skills.”

More information is available at [bioscicareers.stanford.edu](http://bioscicareers.stanford.edu). ISM

## OF NOTE

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

**ELIZABETH EGAN**, MD, PhD, assistant professor of pediatrics and of microbiology and immunology, will receive a 2018 Young Investigator Award from the American Society for Microbiology. The honor, which includes a travel stipend, recognizes early career scientists for research excellence and potential in the fields of microbiology and infectious disease. She is studying the role of the human erythrocyte in host susceptibility to malaria.

**SHANE LIDDELOW**, PhD, a research scientist in neurobiology, and **ANCA PASCA**, MD, a postdoctoral scholar in neonatology, were named 2017 STAT Wunderkinds by STAT News, an online biomedical news organization. Liddelwlow examines the role of astrocytes in central nervous system injury and neurodegenerative disease, with the goal of developing new therapies. Pasca has developed a model of a preterm brain to study neurodevelopmental problems in preterm babies.

**SERGIU PASCA**, MD, assistant professor of psychiatry and behavioral sciences, and **GREGORY SCHERRER**, PhD, PharmD, assistant professor of anesthesiology, perioperative and pain medicine and of neurosurgery, were named 2017 New York Stem Cell Foundation Robertson Investigators. The awards, which include \$1.5 million in seed funding for each recipient, recognize early career scientists

whose innovative research has the potential to lead to improved therapies. Pasca, one of three stem cell investigators to receive the award, develops new approaches for studying hu-

man brain development and examining the mechanisms of neuropsychiatric disorders. Scherrer, one of three neuroscience investigators getting the award, is working to eliminate the brain’s interpretation of pain as unpleasant and identify new ways to treat pain more efficiently and safely than currently done with opioids.

**COURTNEY PEDERSEN**, **MARGOT ROBINSON** and **HANNAH WILD**, who are medical students at Stanford, were awarded 2017 Benjamin H. Kean Travel Fellowships in Tropical Medicine from the American Society of Tropical Medicine and Hygiene. The fellowship provides airfare and \$1,000 in living expenses for clinical training or a research project in an area affected by tropical diseases. Pedersen’s project examined the prevalence and impact of atopic diseases among children under the age of 5 and their families in rural Bangladesh. Robinson’s project evaluated pediatric tuberculosis screening strategies in a community with a high TB rate in South Africa. Wild traveled to Ethiopia’s remote Omo Valley to design and test methods for monitoring the health status of nomadic pastoralists.

**JOHN RATLIFF**, MD, was promoted to professor of neurosurgery, effective July 1. His research focuses on quality improvement, decreasing complications in spine surgery and improving surgical treatment of intramedullary spinal cord tumors. He is the vice chair of neurosurgery and co-director of the Division of Spine and Peripheral Nerve Surgery.

**MAYA ROSSIN-SLATER**, PhD, was appointed assistant professor of health research and policy, effective Sept. 1. Her research interests include maternal and child well-being, family structure and behavior, and policies targeting disadvantaged populations in the United States and other developed countries.

**ERIC SIBLEY**, MD, PhD, associate professor of pediatrics and assistant dean for academic advising, received the 2017 Distinguished Service Award from the North American Society for Pediatric Gastroenterology, Hepatology and Nu-

## Stanford receives grant to create center for support of cancer immunotherapy

The School of Medicine is one of four institutions to receive a grant from the National Cancer Institute to establish a Center for the Immune Monitoring and Analysis of Cancer. Together, the centers will form a network of laboratories to support adult and pediatric immunotherapy trials by analyzing patients’ immune phenotype and function and performing deep tumor profiling.

The grant provides the Stanford center approximately \$12.5 million over five years. It will be headed by Holden Maecker, PhD, professor of microbiology and immunology, and director of the Stanford Human Immune Monitoring Center; and Sean Bendall, PhD, assistant professor of pathology.

Other recipients of the CIMAC grants are the Dana-Farber Cancer Institute, the Icahn School of Medicine



Holden Maecker



Sean Bendall

at Mount Sinai and the MD Anderson Cancer Center at the University of Texas.

The grants were announced by the National Cancer Institute as part of its \$215 million Partnership for Accelerating Cancer Therapies effort, which is a public-private collaboration between the National Institutes of Health and 11 biopharmaceutical companies. The partnership is part of the NIH’s Cancer Moonshot. ISM

trition. The award honors society members who have made major contributions to the field. He investigates the spatiotemporal regulation of genes expressed in the intestine and associated with nutrient assimilation.

**MANJULA TAMURA**, MD, was promoted to professor of medicine, effective Aug. 1. Her primary interest is in improving the quality of end-stage renal disease care among older adults. Her work aims to describe outcomes in older patients and to compare the effectiveness of different management strategies on these outcomes.

**CAPUCINE VAN RECHEM**, PhD, was appointed assistant professor of pathology, effective Sept. 1. Her work focuses on understanding the effects of chromatin modifiers on cancer development and

progression with the goal of developing therapies.

**WILLIAM WEIS**, PhD, the William M. Hume Professor, professor and chair of structural biology and professor of photon science and of molecular and cellular physiology, and **GEORGIOS SKINIOTIS**, PhD, professor of molecular and cellular physiology and of structural biology, were named Innovation Fund Investigators by the Pew Charitable Trusts. This new program promotes collaborative research between alumni of the Pew scholars and fellows programs. Each partnership award provides \$200,000 over two years. Weis and Skiniotis plan to determine the 3-D structure of a signaling complex in the Wnt pathway, which is involved in cellular development and cancer. ISM



Elizabeth Egan



Shane Liddelwlow



Anca Pasca



Sergiu Pasca



Gregory Scherrer



Courtney Pedersen



Margot Robinson



Hannah Wild



John Ratliff



Maya Rossin-Slater



Eric Sibley



Manjula Tamura



Capucine Van Rechem



William Weis



Georgios Skiniotis