INSIDE STANFORD MEDICINE

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If you have ever wondered why some parakeets are green and others are blue, researchers now have an answer for you.

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New graduate students suit up for the future

By Tracie White

GEORGE NIKITIN

William Talbot, senior associate dean for graduate education and postdoctoral affairs, helps graduate student Stephanie Kabeche into her lab coat at a ceremony Sept. 25. Lila Hope (left) is president of the Stanford Medicine Alumni Association, which sponsors the event.

The School of Medicine set recruitment records with this year's new class of doctoral students, receiving the largest-ever pool of applicants and boasting the highest acceptance rate in the school's history.

Of the 2,030 applicants to Stanford's biosciences PhD programs, 174 were offered admission and 116 accepted, according to William Talbot, PhD, the medical school's senior associate dean for graduate education and postdoctoral affairs.

"We look for people who take risks, are creative, work hard and have integrity," he said. "We look for people who are going to be leaders."

Talbot and Lloyd Minor, MD, dean of the School of Medicine, welcomed the new students on Sept. 25, the first day of classes, during a ceremony where they were presented with lab coats.

"Welcome to all of you as you begin what will be one of the most significant journeys of your lives," Minor said, addressing the students gathered at the Li Ka Shing Center for Learning and Knowledge.

This class is also one of the most diverse in the school's history, with 25 percent of new doctoral students coming from underrepresented backgrounds in the biosciences. "Diversity has been a major focus of the dean and of our team," Talbot said. The school has increased outreach programs, recruitment visits across the country and community building to provide a welcoming environment for all students in an effort to increase its diversity levels, he said.

In addition to the 116 new doctoral students, 64 students seeking master's degrees in the biosciences have started their coursework.

Independent funding model

This year, the student yield — the percentage of applicants who accepted offers — was extraordinarily high, Talbot said. Sixty-seven percent

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Hospital discharges for prescription opioids down, but heroin discharges surging, according to researchers

By Tracie White

Hospital discharges related to prescription opioids have declined slightly in recent years, but heroin-related discharges have surged, according to a new study led by researchers at the School of Medicine.

"This suggests that the expanded availability of lethal illicit drugs are being used to replace prescription opioids in some cases," said Tina Hernandez-Boussard, PhD, associate professor of medicine, of biomedical data sciences and of surgery at Stanford. The decrease in hospital discharges due to prescribed opioids could be an indication that initiatives to curtail their over-prescription are beginning to work, she said.

Tina Hernandez-Boussard

The study was published Oct. 2 in *Health Affairs*. Hernandez-Boussard is the senior author. Former Stanford postdoctoral scholar Dario Tedesco, PhD, is the lead author.

The study showed that discharge rates for prescription opioid poisonings declined annually by about 5 percent from 2010 to 2014 while discharges for heroin poisoning increased at an annual rate of 31.4 percent from 2008 to 2014.

The findings add evidence to recent public health concerns that individuals misusing or addicted to prescription opioids are switching to heroin and synthetic opioids, such as fentanyl, because they are cheaper and easier to get, Hernandez-Boussard said. Preliminary statistics from the Centers for Disease Control and Prevention also support this trend, showing that both heroin and synthetic drugs overtook deaths due to prescription opioids in 2016.

Figures remain frighteningly high for all types of opioid use, contributing to what many are calling the worst drug epidemic in United States history, she said. Opioid deaths in the United States now surpass those due to automobile accidents, the study said.

"In the last decade, opioid-related death rates have nearly tripled, opioid-related hospital visits have dramatically increased and misuse of prescription opioids is reaching alarming levels," the study said.

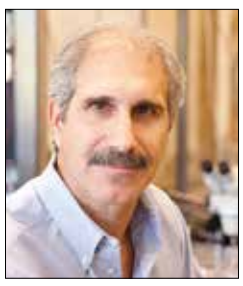
Researchers

See OPIOIDS, page 7

Study shows how 'love hormone' spurs lab mice to be sociable

By Bruce Goldman

Why is it so much fun to hang out with our friends? Why are some people so sociable while others are loners or seemingly outright allergic to interactions with others?



Robert Malenka

A new study by researchers at the School of Medicine begins to provide an answer, pinpointing places and processes in the brains of mice that promote socialization by providing pleasurable sensations when it occurs. The findings point to potential ways of helping people, such as those with autism or schizophrenia, who can be painfully averse to socializing.

The study, which was published Sept. 29 in *Science*, details the role of a substance called oxytocin in fostering and maintaining sociability in mice. The senior author is Robert Malenka, MD, PhD, professor and associate chair of psychiatry and behavioral science. The lead author is former postdoctoral scholar Lin Hung, PhD.

"Our study reveals news about the brain circuitry behind social reward, the positive experience you often get when you run into an old friend or meet somebody you like," said Malenka, who has focused much of his research on an assembly of interacting nerve tracts in the brain collectively known as the reward circuitry.

"The reward circuitry is crucial to our survival because it rewards us for doing things that have, during our evolutionary history, tended to enhance our survival, our reproduction and the survival of our resulting offspring," said Malenka, who holds the Nancy Friend Pritzker Professorship in Psychiatry and the Behavioral Sciences. "It tells us what's good by making us feel good. When you're hungry, food tastes great. When you're thirsty, water is refreshing. Sex is great pretty much most of the time. Hanging out with your friends confers a survival advantage, too, by decreasing your chances of getting eaten by predators, increasing your chances of finding a mate and maybe helping you learn where food and water are."

Reward system conserved

Because

See SOCIABILITY, page 7

Diversity center for School of Medicine opens in Lane Library

STEVE FISCH

Dean Lloyd Minor shakes hands with graduate student Tawaun Lucas at the official opening of the medical school's Diversity Center of Representation and Empowerment at Lane Medical Library.

By Tracie White

When Tawaun Lucas began his graduate studies in 2014 at the School of Medicine, he said he wished there had been a place where he and other minority students could congregate in times of need for support, a physical space for companionship and comfort.

On Oct. 2, the School of Medicine celebrated the opening of just such a place on the ground floor of Lane Library. The Diversity Center of Representation and Empowerment, or CORE, provides a location where any member of the Stanford Medicine community interested in issues of inclusion and diversity can hold meetings or support groups, or just hang out and study. It includes a space for prayer and meditation.

Promoting diversity and inclusion are essential for achieving the goals of Stanford as a world leader in medicine and the biosciences, Lloyd Minor, MD, dean of the School of Medicine, said in remarks at the center's opening.

"We know that in less than a decade, the minority populations in the United States will be the majority," Minor said. "We have to represent the population we serve."

Minor added he believes it's part of his role to work toward these goals "to make us a better community, country and world."

The School of Medicine allocated $10,000 for renovation of the space where CORE is housed, said Mijiza Sanchez, EdD, associate dean for medical student affairs.

Lucas was one of five students who advocated for a diversity center and then worked to make it a reality after Minor committed funds for it.

STEVE FISCH

Students attend the event, which included remarks by Minor and Lucas.

Last summer, concerned about the climate in the country at a time when headlines were dominated by shootings of unarmed black men by police and protest rallies, Lucas said he and fellow students Dorothy Tovar, Shanique Martin, Gabriel Washington and Osama El-Gabalawy joined together to work toward more inclusivity on campus and to provide a welcoming environment for its underrepresented minorities.

'Bigger than medicine'

In the fall of 2016, the five delivered a list of recommendations to the dean, Lucas said. The dean responded immediately to the recommendation to create a diversity center.

At CORE's official opening, the dean and others spoke about the need to continue to work toward goals of diversity on campus and the fundamental rights of treating others with dignity, respect and compassion.

"We all struggle to make sense of the world today," Minor said, noting the recent shootings in Las Vegas and hurricane damage in Puerto Rico. "This community represented by CORE will help us grapple with the issues of today." He also thanked the organizing committee that brought the concept of the diversity center to him.

"These principles are bigger than medicine," said El-Gabalawy, a second-year medical student and one of the founders of the center. "But they are arguably the most important in medicine because we not only have to treat patients from every walk of life, but we are entrusted with the most sacred thing of all: their lives." **ISM**

University launches research center on global poverty, development

Global poverty is one of the most pressing issues of our time. While great progress has been made to combat it in recent decades, nearly 800 million people still live below the international poverty line of $1.90 a day, and more than 2 billion people are on the cusp of poverty. Thanks to technological advances and a rising sense of urgency, researchers, policymakers and business leaders now have an even greater ability to help end global poverty.

To focus more squarely than ever before on this challenge, Stanford University is creating the Stanford Center on Global Poverty and Development. Launched Oct. 2, the center will join students and faculty from across the university and connect them with policymakers and business leaders committed to fighting poverty.

The center's mission is threefold: to support path-breaking research on global poverty and development within Stanford and beyond; to inspire students through hands-on research opportunities, fellowships and events; and to inform policies and practices through strategic partnerships with global policymakers and thought leaders, as well as through on-campus events that foster new ideas and universitywide collaborations.

The center — which has more than 100 affiliated faculty from across the university — is a joint venture between the Stanford Institute for Economic Policy Research, or SIEPR, and the Stanford Institute for Innovation in Developing Economies, known as Stanford Seed. The center continues a number of programs and initiatives formerly housed under Stanford Seed and SIEPR's Stanford Center for International Development.

'Poised to lead'

"Global poverty is extremely complex," said Grant Miller, PhD, the center's director and an associate professor of medicine. "It demands multidisciplinary collaboration and meaningful engagement with decision-makers. Stanford has a culture and proven track record of interdisciplinary research and real-world impact, and it is now poised to lead in work confronting global poverty and promoting development."

The center will expand the scope and pace of research already underway by faculty and students from across the university — experts in economics, political science, sociology, engineering and medicine, among other fields — who are generating insights into the roots of poverty and creating solutions. High-resolution satellite imagery is allowing Stanford researchers to identify and study hidden pockets of poverty around the world in a way not previously possible. A new effort to map and survey employers and their employees in China is shedding light on key labor issues confronting the "factory of the world."

"When insights from studies like these reach people who are shaping policy and practice in the developing world, it can lead to new strategies for alleviating poverty — and it can also stimulate new research with even greater impact," said Mark Duggan, PhD, a professor of economics who holds the Trione Directorship of SIEPR and the Wayne and Jodi Cooperman Professorship. "Leaders on the front lines of the private sector and government need rigorous data-driven research from which to draw, to help them make decisions that will lead to more innovation and to better policies."

New programs

The center is kicking off several new programs developed and led by multidisciplinary teams of faculty, including:

• **The Data for Development Initiative.** New data from sources like satellite imagery and cell phone records — together with powerful methods for analyzing them — are radically reshaping development research and strategies for building sustainable economies around the world. Through research collaboration, student training and strategic partnerships, this initiative leverages new data and tools for examining a broad range of questions surrounding poverty, agriculture, infrastructure, migration and other critical issues.

• **The Firms and Global Productivity Initiative.** Despite the important role that businesses play in economic growth and in moving people out of poverty, a lack of high-quality, in-depth data limits what we know about the private sector. This initiative is filling this void through pioneering projects that collect data on key issues, including productivity, job creation and sources of innovation, that are affecting businesses in China, India and other countries.

• **The student experience.** Through opportunities on and off campus, the center is committed to immersing students in issues surrounding global poverty and development — and to inspiring and supporting them as they seek answers and solutions. Through fellowships and mentored research opportunities, students can conduct research on the ground in middle- and low-income countries.

"Ending the cycle of global poverty requires the kind of advances in fundamental knowledge that a research university can generate, and that's what this center is going to provide," said Jesper Sorensen, professor of business, Robert A. and Elizabeth R. Jeffe Professor and faculty director of Stanford Seed. "The fact that we're bringing together not only faculty and students from all parts of the university but collaborating with development experts worldwide is truly inspiring."

To celebrate the launch of the center, an event for supporters and the campus community is set for Nov. 13 and will feature a keynote address by Ngozi Okonjo-Iweala, PhD, chair of the board of Gavi, the Vaccine Alliance; former finance minister of Nigeria; and former managing director of the World Bank Group. **ISM**

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STANFORD MEDICINE

At open house, Integrated Strategic Plan solicits community input

By Becky Bach

Greeted by balloons, boxed lunches and jumbo posters adorned with sticky notes, several hundred members of the Stanford Medicine community gathered Oct. 3 in Berg Hall to share their thoughts on the Integrated Strategic Plan.

The plan will align the priorities of the School of Medicine, Stanford Health Care and Stanford Children's Health and lay out a course for Stanford Medicine's next 20 years. The planning process kicked off early this year with a survey of community priorities and interviews with selected leaders and groups.

Currently, 13 category-based committees are working to answer key questions about Stanford Medicine's future, such as, "How can we best leverage our existing assets to better meet the needs and expectations of the communities we serve?" And "in research, should Stanford Medicine 'let a thousand flowers bloom?'"

In December, the groups will submit white papers addressing these questions, which will then be examined by Stanford Medicine leaders in 2018 and compiled into the final plan, said Nancy Taylor, chief strategy officer for the School of Medicine.

The current planning effort is unique because it is the first in recent history that brings together the adult hospital, children's hospital and the medical school, said Sean Hennessey, senior director for strategy and analytics at the medical school.

The process is timed to contribute to and align with the universitywide strategic planning efforts.

At the open house, the goal was to gather input from community members, Hennessey said. "What can we do better? What's the future ideal look like?" he asked.

ROD SEARCEY

At the Integrated Strategic Plan open house Oct. 3, Renee Cisco, a social work clinician, casts a vote via sticker for an attribute she hopes will characterize Stanford Medicine's culture in 2025.

Seeking ideas from community

Berg Hall was organized to allow attendees to share their thoughts and interact with employees from other areas of Stanford Medicine. Along one wall, a giant poster featured Stanford Medicine's mission and vision statement. Attendees jotted down related thoughts on neon-colored sticky notes. "What happens here at Stanford has the potential to shape the world!" one bright green sticky read.

Another display asked attendees to vote for five of 24 attributes they hope will characterize Stanford Medicine's culture in 2025. A few of the most popular attributes included: valuing and appreciating people; clear direction and leadership; cross-functional and collaborative teamwork; and accountable for performance.

Community members offered a variety of motivations for attending the event. Jayna Rogers, a wellness manager with the Health Improvement Program, said she hopes the plan will enhance Stanford Medicine's focus on preventive health and well-being.

Dale Beatty, DNP, the chief nursing officer at Stanford Health Care, said he attended the event to learn more about the process and to provide feedback. Julie Tisnado, director of clinical services at Stanford Health Care, said she is looking forward to a future in which the two hospitals are more closely affiliated, a sentiment that was shared by Linda Jordan, a manager of advanced practices at Stanford Children's Health. "We are very interested in working together," she said.

The time to submit ideas for the Integrated Strategic Plan is now, Taylor said. She urged anyone with contributions or questions to reach out to integratedstrategy@stanford.edu.

The website http://med.stanford.edu/isp.html provides additional information. In addition, the plan will be discussed at the State of Stanford Medicine forum scheduled for noon to 1 p.m. Oct. 24 in Berg Hall. **ISM**

After medical error, revealing facts, offering apology goes a long way

By Beth Duff-Brown

Sometimes a straightforward explanation and an apology for what went wrong in the hospital goes a long way toward preventing medical malpractice litigation and improving patient safety.

That's what Michelle Mello, JD, PhD, and her colleagues found in a study published Oct. 2 in *Health Affairs*.

Mello, a professor of health research and policy and of law at Stanford, is the lead author of the study. The senior author is Kenneth Sands, former senior vice president at Beth Israel Deaconess Medical Center.

Medical injuries are a leading cause of death in the United States. The lawsuits they spawn are also a major concern for physicians and health care facilities. So, hospital risk managers and liability insurers are experimenting with new approaches to resolving these disputes that channel them away from litigation.

ALEXANDER RATHS / SHUTTERSTOCK.COM

New research shows that discussing hospital errors with patients leads to better patient safety without spurring a barrage of malpractice claims.

The focus is on meeting patients' needs without requiring them to sue. Hospitals disclose accidents to patients, investigate and explain why they occurred, apologize and, in cases in which the harm was due to a medical error, offer compensation and reassurance that steps will be taken to keep it from happening again.

Positive results

The study reports on the outcome of a so-called communication-and-resolution program at two large Massachusetts hospital systems. Mello and her co-authors found that the program not only yielded positive results in terms of liability costs but also led to significant patient safety improvements.

"In these programs, hospitals scrutinize every serious harm event to answer the question, 'What can we learn?'" Mello said. "Traditionally, a risk manager's focus has been on the patients who complain about the care or threaten to sue. But every patient deserves to know that what happened to them is being taken seriously."

Despite concerns that telling patients about errors and proactively offering compensation could cause liability costs to skyrocket, of the 989 adverse events reviewed for the study from 2013 to 2015, only 5 percent led to malpractice claims or lawsuits. And when the program did lead to compensation, the median payment was $75,000. By comparison, the median payment nationwide in 2015 when plaintiffs prevailed in malpractice lawsuits was about $225,000, Mello noted.

Michelle Mello

"Our findings suggest that communication-and-resolution programs will not lead to higher liability costs when hospitals adhere to their commitment to offer compensation proactively," the authors wrote.

Pilot program

The authors focused on a program called CARe — Communication, Apology and Resolution — at six Massachusetts hospitals: Beth Israel Deaconess Medical Center and Baystate Medical Center, and two of each center's community hospitals.

The hospitals demonstrated good adherence to the program protocol, the authors found. Physicians were supportive of the approach, but did ask for better communication about the program and what was happening with their patients.

The low percentage of events that led to litigation should reassure hospitals concerned about the risks of being honest with patients, the authors wrote. A likely explanation, according to Mello, is that explaining why adverse events occurred defused patients' anger. About three-quarters of the time, adverse events were not actually due to error, the study said. Rather, malpractice claims frequently arise when plaintiffs perceive that the health care providers communicated poorly or attempted to cover up negligence, the authors noted.

"Given the rarity with which communication-and-resolution events resulted in settlements, it is reasonable to wonder whether the programs are worth the time they require," the authors wrote, "but risk managers in our study thought they were. By providing explanations and expressions of sympathy for harms not arising from negligence, communication-and-resolution programs may avert lawsuits springing from misunderstanding."

One objective: improve patient safety

The CARe objectives are to improve transparency surrounding events, improve patient safety, reduce lawsuits and support clinicians in disclosing error or injury.

Medical events were bumped to a CARe evaluation if they met a severity threshold of either causing permanent or temporary harm that led to an extended hospitalization, required an invasive procedure or led to at least three outpatient visits.

Of the 989 total events studied by the authors, 60 of them entered the CARe program because the hospital received notice that the patient intended to sue. Another 929 entered the program when an adverse event was reported that allegedly exceeded the severity threshold, or that met other criteria.

The protocol called for compensation to be proactively offered whenever a violation of the standard of care caused serious harm. Only 9 percent of cases met these criteria. The largest payment made was $2 million. In 181 events, mostly events for which compensation criteria weren't met, hospitals offered to waive medical bills or made other modest gestures, like giving the patients meal vouchers and gift cards. About three-quarters of injuries didn't qualify for compensation because the standard of care was judged to have been met — a proportion that is consistent with prior studies of medical injuries. About a third of the injuries weren't caused by the medical care: For example, a patient contracted an infection in the hospital but died from other causes.

"These programs are usually talked about as a way to resolve cases of medical error, but what they do more often is encourage communication with patients about non-error events — as well as systematic evaluation of each event for patient-safety lessons," Mello said.

The authors also noted that communication-and-resolution programs "can help hospitals foster a culture of transparency by supporting clinicians in making disclosures."

The safety interventions identified in the CARe investigations included new labeling for high-risk medications, color-coded socks for patients at risk for falls, radio frequency identification tags for surgical sponges, improved interpreter services, improvements for managing the selection of implantables after surgery, and a multidisciplinary checklist for breech deliveries.

Other authors of the study are affiliated with Harvard, Tufts, Baystate Medical Center, and Beth Israel Deaconess Medical Center.

The study was funded by Baystate Health Insurance Company, Blue Cross Blue Shield of Massachusetts, CRICO RMF, Coverys, Harvard Pilgrim Health Care, Massachusetts Medical Society and Tufts Health Plan.

ISM

Biobank and foundation team up to accelerate research into a rare disease

By Kris Newby

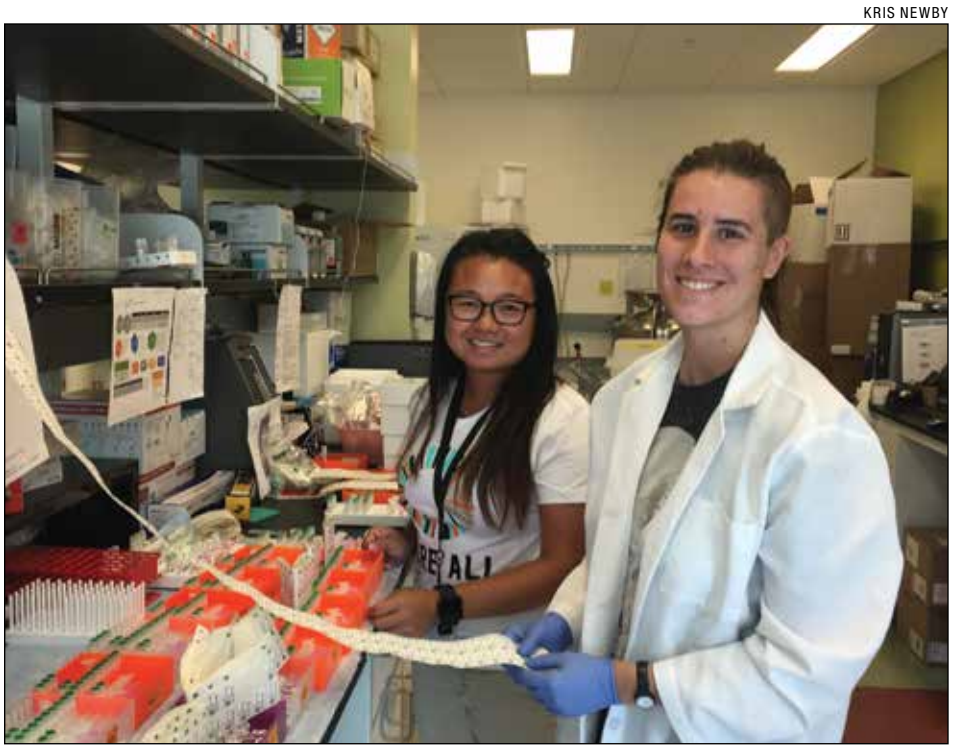
Medical research is a numbers game: Funding often goes to those diseases with the largest number of patients. But what if your child is one of 36 born with a rare genetic disease?

In late July, the Grace Science Foundation and a clinical research team from Stanford University piloted a novel way to accelerate research into the rare NGLY1 gene defect. In just a few days, they collected health data and samples from 20 of the 36 living patients and members of their families, then cataloged them into a "lending library" of linked biological samples, genomic information and medical records. Now, any researcher interested in this or related defects can request access to this open-source data without the costs associated with patient recruitment, sample collection and biobanking.

The founders of Grace Science Foundation, Matt and Kristen Wilsey, started this nonprofit four years ago after their daughter, Grace, was diagnosed with this rare genetic disorder. It is inherited when both parents pass on a defective copy of the NGLY1 gene.

NGLY1 stands for N-glycanase 1. The gene tells the body how to produce an enzyme that removes sugar molecules called glycans from misfolded proteins so that the proteins can be used in key biochemical processes. When a person doesn't produce enough of the enzyme, the process is severely disrupted. Shortly after birth, the affected individuals develop movement disorders, delayed growth, seizures, dry eyes and liver problems.

KRIS NEWBY



Janine Sung and Rebecca Giessler helped make sure biological samples from the patients and members of their families were properly labeled, de-identified, processed and stored in a biobank at Stanford.

CARRIE CHEN PHOTOGRAPHY

KRIS NEWBY

(Above) Kristen and Matt Wilsey started a foundation four years ago to support research into NGLY1 deficiency after their daughter, Grace, was diagnosed with the disease. The foundation has joined forces with Stanford to accelerate research into the rare gene defect. (Right) Laila Craveiro, center, oversaw efforts to collect biosamples from patients and their families. Ciara Miranda, left, and Kristin Barone, right, drew blood samples.

No time to wait

The Wilseys realized that Grace and the other individuals with NGLY1 deficiency could not wait the decades that it normally takes to find treatments for a newly discovered disease. Several patients have died before reaching adulthood. So, Matt Wilsey applied the strategy that he'd used as a tech entrepreneur building fast-moving startups in Silicon Valley: He assembled a team of experts, provided them with funding, then urged them to share findings early and often. By fostering trust and collaboration, scientists from different institutions could build on one another's ideas more quickly, short-circuiting the many months that it takes to write up a study and submit it to journals for open publication.

Among the experts Wilsey recruited was Rohit Gupta, director of the biobank and clinical research services under Spectrum, the Stanford Center for Clinical and Translational Research and Education. At that time, Gupta was breaking in a new system for storing, tracking and sharing biological samples. He and Gupta brainstormed about how they could join forces and use the new biobank to speed up the slowest and most inefficient phases of any human-subject study: participant recruitment and sample collection.

Typically, it takes months to years for a researcher to find enough target patients from whom to collect biological specimens and data. (For many rare diseases, a researcher may never find enough patients to justify starting the analysis phase of a study.)

'A challenging event'

Through meticulous planning, the Wilseys and the Stanford team designed a streamlined process to collect biospecimens and health data in just a few days. Patient recruiting and logistics were orchestrated by the Grace Science Foundation and Shannon Rego, MS, a genetic counselor in the lab of Michael Snyder, PhD, professor and chair of genetics. Leveraging its communications channels, the foundation invited NGLY1 families to its annual scientific conference in July in Palo Alto, with the promise of meeting researchers face-to-face and participating in a study that might accelerate treatments and cures.

Once they arrived, Laila Craveiro, the nurse manager of the Spectrum clinical services unit, oversaw 18 nurses, phlebotomists, coordinators and physicians in collecting 325 skin, urine, stool, blood and DNA samples.

"It was a challenging event," said Craveiro. "Two children had seizures. Many were in wheelchairs. At the end of weekend, we were bone-tired but happy to be a part of this significant event."

Before the collection event, the unit's staff created color-coded labels to avoid mixing up samples of family members with the same last name. They had to line up couriers to transport time-sensitive samples to the biobank facility for processing in under an hour. And the Grace Science Foundation found volunteers to translate for the families who spoke Portuguese, German, French, Spanish, Danish, Hebrew and Chinese.

> "This biobank is a tremendous step forward to curing NGLY1 deficiency."

Back at the biobank, lab technicians went beyond standard specimen-processing methods to isolate and preserve cells and fluids from the collected samples. This centralized sharing approach also minimizes the error associated with the inherent variability in sample collection and processing methods. Each specimen was labeled with de-identified tags and logged into the biobank warehouse so that they could be retrieved as needed from a freezer array managed by Janine Sung, the Spectrum biobank officer.

To accelerate analysis and discovery, the NGLY1 samples now can be requested by researchers through a web-based catalog hosted at Stanford. A governance board of Stanford and the Grace Science Foundation representatives reviews requests.

Researchers can search the catalog and request age-, sex- and condition-matched specimens for analysis. Ultimately, researchers will also be able to download de-identified clinical and assay data sets to apply new, advanced bioinformatics approaches to looking at this patient population.

At Stanford, Snyder will lead the genetic sequencing of each participant's gut microbiome. Guangwen (Gavin) Wang, PhD, director of the Stem Cell Core Facility in the Department of Genetics, will grow an NGLY1 stem cell line from the tissue biopsies. And Gregory Enns, MB, ChB, professor of pediatric genetics, will be working with researchers from other institutions around the world to analyze the genomic, metabolic and health-questionnaire data. They will be looking for ideas for early diagnosis and potential treatments.

"This effort will make a huge difference not only for our understanding of this rare disease, but also for insights into other, more common disorders, because the NGLY1 enzyme is critical to normal cellular metabolism," Enns said.

Another researcher who is working on understanding the biochemical mechanisms behind NGLY1 deficiency is Carolyn Bertozzi, PhD, professor of chemistry and ChEM-H faculty fellow. She is working on a study that suggests forcing an NGLY1 deficiency in a cancer patient may keep tumors from becoming resistant to certain treatments.

Wilsey and Gupta said they were so pleased with the way the NGLY1 event worked that they'd like to find ways to facilitate this approach for other conditions.

"This biobank is a tremendous step forward to curing NGLY1 deficiency," Wilsey said. "We can't thank the Stanford team enough for their heroic efforts. We firmly believe what we did is the new model that other organizations can follow."

"Modern day biobanks are critical to accelerating global efforts in precision health," said Gupta. "They link unique biological specimens to databases of associated clinical and assay data. This provides researchers with immediate access to cohort-matched samples, which ultimately advances biomarker research and future diagnostics and therapeutics."

For questions about the biobank or getting access to NGLY1 samples, contact Sung at jsung3@stanford.edu. ISM

Stanford staffer jumps back into research with help of NIH grant

By Kris Newby

In 2011, Anandi Krishnan, PhD, was on the fast track to a promising academic research career.

A research fellow at Duke University, she had earned a PhD in bioengineering from Penn State in less than four years and was the lead author of 11 scientific papers. But a complicated pregnancy, an illness in her family and time off to care for her newborn child derailed her plans.

While she feared that the extended leave might end her research career, she was awarded a National Institutes of Health career re-entry grant in 2016 that enabled her to move from a staff position at Stanford back into research.

After she returned from her family leave in 2012, Krishnan and her husband, a postdoctoral scholar, faced the difficulty of landing jobs at the same university. Faculty research positions are scarce, and the competition for NIH grants is fierce. To increase their odds of success, the couple decided to relocate to the job-rich San Francisco Bay Area. Krishnan took a staff position in 2012 as the academic and research program officer at Spectrum, the Stanford Center for Clinical and Translational Research and Education, and the family moved to Palo Alto.

Missing research

Krishnan said she enjoyed her role at Stanford in educating young scholars on clinical and translational research. But over time, she found herself missing hands-on research. Then, through Spectrum, she heard about a new career re-entry program funded by the NIH's Clinical and Translational Science Awards Program. She applied in 2016, and six months later, she had the funding to start again.

Called a "re-entry supplement," the program funds the salary of investigators whose careers have been interrupted for one to eight years for unavoidable reasons. Examples of qualifying interruptions could include child-rearing, an incapacitating personal or family illness, a spouse relocation or military service.

"It was like the grant had been written specifically for my situation," Krishnan said.

To apply, Krishnan first had to identify a mentor and lab space. Then she had to write a short research plan, draft a mentoring and career-development plan, and obtain letters of support. Stanford faculty and staff rallied to help.

James Zehnder, MD, professor of pathology and of medicine, agreed to be her mentor. When awarded the re-entry grant, the Pathology Department offered her an instructor position.

COURTESY OF ANANDI KRISHNAN

A career re-entry grant from the National Institutes of Health helped Anandi Krishnan resume her research. She's studying blood platelet gene markers in patients with myeloproliferative neoplasms.

Krishnan decided to focus her current research on looking for blood platelet gene markers in patients with myeloproliferative neoplasms, or MPNs, which are blood cancers that cause too many white or red blood cells or platelets to be produced in the body. Such markers could be used to diagnose and assess treatments in MPN patients.

Thrilled to do research again

"Platelets are understudied when it comes to blood cancers," said Krishnan. "They aren't simply sacks of glue that stop bleeding."

Jason Gotlib, MD, professor of hematology, is advising her on her research and providing her with staff support for access to his MPN patient data registry.

Krishnan said she is thrilled to be back doing research, and is busy working in her new lab and expanding her bioinformatics skills. As she finishes her first year since receiving the re-entry grant, she's putting the finishing touches on a new research paper and using her preliminary data to apply for more research grants. (She was recently awarded a research grant from the Pathology Department.)

"I am thankful to the various Stanford faculty and staff who helped me secure this unique opportunity and look forward to guiding the careers of others who might be navigating similar life-related interruptions," Krishnan said. **ISM**

A tale of cacao, birds and the 'power of emerging model systems'

By Nathan Collins

If you have ever wondered why some parakeets are green and others are blue, Stanford researchers now have an answer for you.

And, the scientists say, the techniques they developed in the process could one day lead to the discovery of new chemical compounds or biomolecular processes that could impact human health.

The endeavor began over dinner, with a discussion of chocolate — specifically, the domestication of chocolate's main ingredient, cacao. Thomas Cooke, PhD, then a graduate student in genetics, had been working on tools to study "non-model organisms," — plants and animals that get less attention than lab rats, fruit flies or baker's yeast — despite their potential for yielding important scientific insights. Cooke had been working on cacao, but he said the project had "fizzled," and he was looking for what to do next.

He was discussing his situation at a Palo Alto diner with biochemistry graduate student Kathleen Xie, who mentioned a peculiar trait of the budgerigars she'd raised growing up: wild budgies are green and yellow, but others have been bred since the 19th century to be blue and white — and no one knew exactly how, on a genetic or molecular level, that happened.

A Mendelian trait

Cooke, Xie and colleagues set out to figure out what was in some ways the perfect test case for the methods Cooke had been working on. It had been known for years that wild budgies' color came from a yellow pigment the budgies themselves produce, and it had been known even longer that their color was a Mendelian trait; that is, budgies either made the yellow pigment or they didn't. It should therefore be straightforward, if not exactly easy, to track down the gene responsible for determining budgie color.

Working with Stanford ChEM-H's 1-year-old Metabolic Chemistry Analysis Center and researchers from around the chemical and life sciences — and members of the American Budgerigar Society and the Budgerigar Association of America, who provided samples and advice — Cooke tracked blue budgies' color to a gene encoding a protein they dubbed MuPKS, for *Melopsittacus undulatas* polyketide synthase. (*Melopsittacus undulatas* is the budgie's binomial name.) A change to just one amino acid in MuPKS, the researchers found, stops budgies from producing yellow pigment, revealing an underlying blue color in the birds' feathers. To confirm those results, the team next transferred the MuPKS gene into baker's yeast and showed that the yellow variant turned yeast yellow, while the other variant had no effect on color.

Their findings were published Oct. 5 in *Cell*. Cooke, who will soon begin a postdoctoral fellowship at the Massachusetts Institute of Technology, is the lead author.

Study is a harbinger

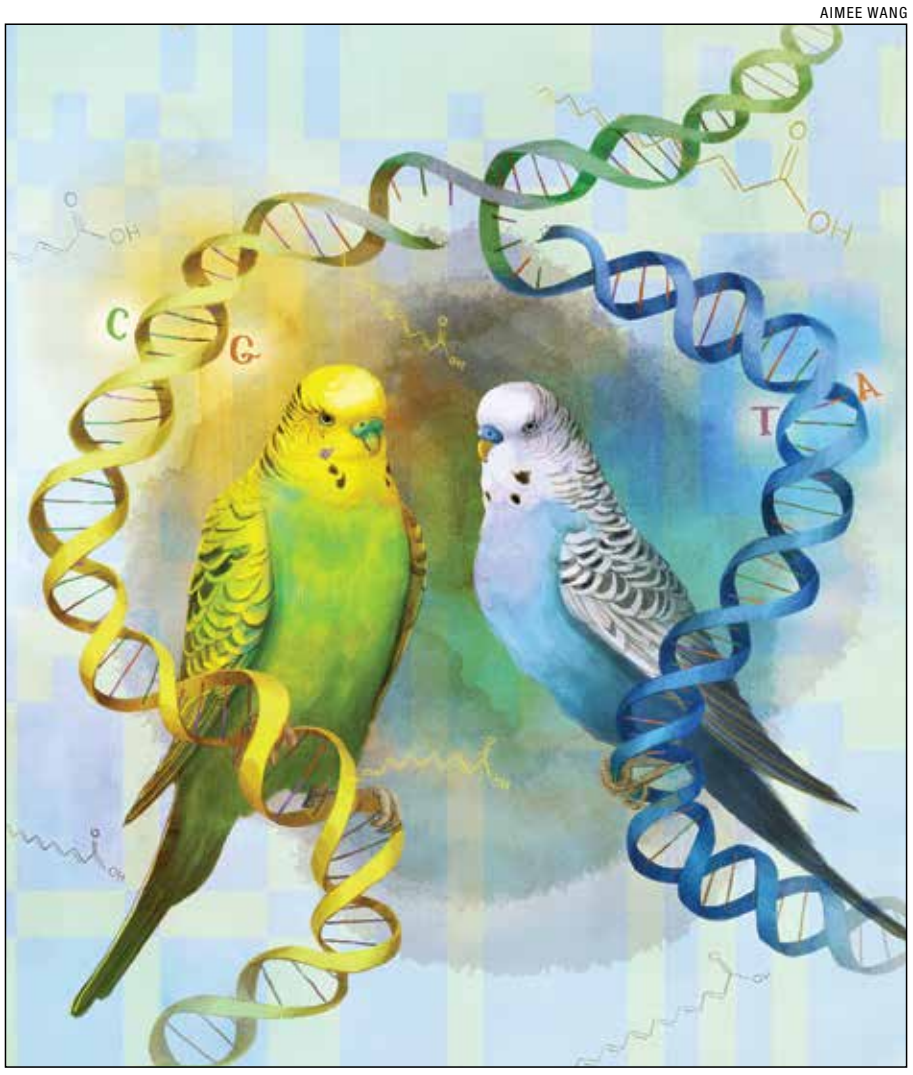
Even if parakeet color itself doesn't turn out to be the most interesting subject scientifically, the study is harbinger of things to come, said Carlos Bustamante, PhD, professor of biomedical data science and of genetics and one of the paper's senior authors.

"What Thomas conceptually demonstrated was we could go into any organism" and learn something interesting and useful about its biochemistry, Bustamante said.

In the future, the techniques Cooke developed — and the ever-declining cost of genetics research in general — could help scientists look at many different plants and animals at once, increasing the likelihood someone will find the next key medicinal compound or biochemical pathway sooner rather than later. "It really demonstrates the power of emerging model systems," Bustamante said.

"To me, the highlight of the story is Tom Cooke," said study co-author Chaitan Khosla, PhD, professor of chemistry and of chemical engineering and director of ChEM-H. Cooke and his work, Khosla said, exemplify a new approach to life sciences that bridges work in genetics, biochemistry and other fields.

AIMEE WANG



Researchers traced blue budgies' color to a variation in a protein called MuPKS.

Additional Stanford co-authors include Curt Fischer, PhD, research engineer; former graduate student James Kuo, PhD; Elizabeth Doctorov, a high school intern at the time of the research and now a sophomore at UC-Berkeley; and Ashley Zehnder, DVM, PhD, research scientist.

The study was funded by the National Institutes of Health.

Stanford's departments of Genetics, of Biochemistry, of Biomedical Data Science, of Chemical Engineering and of Chemistry also supported the work. **ISM**

Five researchers receive NIH funding for innovative projects

Five Stanford scientists who want to delve deeper into the workings of our tissues, our immune systems, our brains and our guts have received $13.25 million from the National Institutes of Health to fund their innovative projects.

They are among the 86 scientists nationwide to receive Pioneer, New Innovator, Early Independence and Transformative Research awards through the NIH's High-Risk, High-Reward Research program. This year's awards total $263 million.

Three of the Stanford scientists received Pioneer Awards, one received a New Innovator Award and another received an Early Independence Award. Four of the recipients are from the School of Medicine, while the fifth is from the School of Humanities & Sciences.

"Addressing today's complex challenges in human health requires taking bold and innovative risks," said Lloyd Minor, MD, dean of the School of Medicine. "I am thrilled that four of our scientists received recognition for unconventional, exemplary work that will bring us closer to delivering predictive and preventive care to all."

Pioneer Award

The Pioneer Award provides up to $3.5 million, dispensed over five years, to investigators at all career levels to pursue new research directions and develop groundbreaking, high-impact approaches to a broad area of biomedical or behavioral science.

Hongjie Dai, PhD, professor of chemistry, plans to use the award to develop infrared-emitting probes through nanoscience and chemical principles to enable deep-tissue, real-time, in-vivo imaging down to cellular resolution.

"Such infrared vision will be employed to address fundamental and practical problems in neuroscience, cancer and cardiovascular diseases," Dai said.

Dai works at the interface of nanochemistry, materials sciences and biomedical sciences. In recent years, he has led the development of a fluorescence-imaging technique that can produce images of blood vessels in the hind limbs and brains of living mice with unprecedented clarity in the near-infrared regime. This technique works by injecting a dye into the animal's bloodstream that fluoresces near-infrared light beyond 1,000 nanometers.

Hongjie Dai

Dai plans to use the grant to push the imaging technique further toward the infrared regime, which would result in even clearer images that can be produced from greater depths within tissues. With this enhanced capability, researchers may be able to use this imaging technique in animal models and eventually inhumans, where it could help with basic understanding of diseases and lead to potentially better diagnostics and treatments.

Dai is a member of Stanford Bio-X, the Stanford Biophysics Program, the Stanford Cardiovascular Institute, the Stanford Child Health Research Institute, the Stanford Cancer Institute and the Stanford Neurosciences Institute.

Amit Etkin, MD, PhD, associate professor of psychiatry and behavioral sciences, researches the neural basis of mental disorders and their treatment. His overarching goal is to transform the diagnosis and treatment of various psychiatric ailments through neurobiology.

Amit Etkin

He will use his Pioneer Award to further explore what is malfunctioning in the brains of individual patients and then construct interventions using noninvasive tools that stimulate cells deep inside the brain while recording responses with imaging tools such as an electroencephalogram, a test that detects electrical activity in the brain.

In addition to building new physical tools, his goal is to develop more powerful data-analytic approaches to provide more precise information on how individual brains function.

After developing a new diagnostic and interventional platform based on understanding brain dysfunction among individual patients, Etkin plans to conduct clinical trials of these individualized, tailored interventions and then generalize this approach for use across the field of psychiatry for patients with various mental health disorders.

Etkin is also an investigator at the Sierra-Pacific Mental Illness Research Education and Clinical Center at the Veterans Affairs Palo Alto Health Care System. He is a member of Stanford Bio-X and the Stanford Neurosciences Institute.

Justin Sonnenburg, PhD, associate professor of microbiology and immunology, concentrates on the microbiome, the complex community of microbes that lives in our gut. "A person is not just a collection of human cells," he said. "Each of us is a walking ecosystem composed of thousands of microbial species in addition to ours."

Justin Sonnenburg

Over even relatively short periods of time, a person's gut microbes can change — for example, due to dietary change; over generations, so can an entire population's. Recent studies by Sonnenburg and others suggest that the microbiome of industrialized populations, whose diet is rich in highly processed foods and low in fiber, is deficient to some degree, compared with that of traditional hunter-gatherer populations whose fiber-packed diets closely resemble those of our evolutionary ancestors. This deficiency may be predisposing inhabitants of modern urban societies toward certain diseases.

Sonnenburg intends to use the award to analyze diverse populations' microbiomes in an effort to further define what constitutes a healthy microbiome, and to what extent features of that microbiome that have been lost during modernization may be affecting human health.

He is a member of Stanford Bio-X and of Stanford ChEM-H, and co-director of the medical school's Center for Human Microbiome Studies.

New Innovator Award

Lingyin Li, PhD, assistant professor of biochemistry, received a New Innovator Award, which provides up to $1.5 million over five years to fund innovative research by investigators who are within 10 years of their final degree or clinical residency and who have not yet received a research project grant or the equivalent from the NIH.

Li focuses on understanding how the innate immune system works and how to harness it to treat diseases such as cancer. She intends to use her award to conduct fundamental mechanistic studies and, in parallel, identify promising anti-cancer drug targets and develop drug leads as novel immunotherapeutics.

"This money is a lifesaver for my lab to conduct proof-of-concept experiments along these lines," she said. "Because our research spans basic biochemistry, molecular biology, cancer immunology and drug development, it falls outside the purview of traditional funding mechanisms."

Recent breakthroughs in treating cancer by harnessing the adaptive immune system have been very effective in a small percentage of patients with limited kinds of cancers. It's generally believed, Li said, that by increasing innate immune recognition of the remaining cancer types, oncologists might be able to treat those cancers more effectively, as well. But exactly how the innate immune system recognizes cancer is poorly understood. Li's lab aims to uncover these mechanisms and target them with drugs.

Lingyin Li

Li is a member of Stanford Bio-X and is a Stanford ChEM-H institute scholar.

Early Independence Award

Kyle Loh, PhD, instructor in stem cell biology, received an Early Independence Award, which supports promising young investigators with up to $1.25 million over five years. The awards allow exceptional early career scientists who have recently received their doctoral degree or completed their medical residency to skip traditional postdoctoral training and move immediately into independent research positions.

Loh is working to find ways to grow transplantable human cells or organs in the laboratory from cultured, pluripotent stem cells, eliminating the need for a human donor. He also hopes to devise ways to manipulate the human immune system to remove the need for tissue recipients to undergo long-term immune suppression to prevent transplant rejection.

Kyle Loh

He plans to use the award to help him establish an independent laboratory and to pursue the goal of making human tissue and organ transplantation safer and more readily available.

Loh is a member of the Stanford Institute for Stem Cell Biology and Regenerative Medicine.

The funders of this year's awards are the NIH Common Fund, National Institute of General Medical Sciences, National Institute of Mental Health, National Center for Complementary and Integrative Health and National Institute of Dental and Craniofacial Research. ISM

Faculty members, postdocs, medical students receive clinical research training awards

Eleven young faculty members, postdoctoral scholars and medical students have been selected to participate in one of two National Institutes of Health-funded programs designed to advance their careers as clinical and translational researchers.

Universitywide, these two programs are administered by Spectrum, the Stanford Center for Clinical and Translational Research and Education. Both programs provide promising young scholars with financial support, training and mentoring to help them initiate research that accelerates the translation of medical discoveries into better health.

KL2 program

Five scholars will join the KL2 Mentored Career Development Program, which provides senior fellows and junior faculty in health-related professions with financial support and advanced training in clinical and translational research. The new KL2 program participants are:

- Tessa Andermann, MD, MPH, infectious diseases
- Matthew Baker, MD, immunology and rheumatology
- Allison Kwong, MD, gastroenterology and hepatology
- Adam Miner, PsyD, internal medicine
- Lindsay Sceats, MD, resident, surgery

TL1 program

Another six have been accepted into the TL1 Predoctoral and Postdoctoral Research Training Program, which provides participants with partial tuition and stipend support for a year of full-time instruction in research methods or protected time for research. The new TL1 program participants are:

- Brian Boursiquot, student, biomedical engineering and medicine
- Andrew Chang, MD, instructor, general medical disciplines
- Jack Ching, PhD student, health research and policy
- Nathan Itoga, MD, resident, vascular surgery
- Sheldon Leong, MD, fellow, nephrology
- Benjamin Lerman, medical student

Both programs are funded by an institutional Clinical and Translational Science Award from the NIH.

Information on these programs is available on the Spectrum website at http://med.stanford.edu/spectrum/b2_education/b3_2_research_training_program.html. ISM

Students

continued from page 1

of the doctoral-program applicants offered admission decided to matriculate at Stanford, a figure that has steadily increased since the school implemented the Biomedical Innovation Initiative. Also known as the independent funding model, the initiative, which was launched in 2013, guarantees PhD students full funding for four years without having to rely on a faculty researcher's funding.

The initiative gives students the freedom to pursue inventive biomedical research, Talbot said. Students are funded by a combination of fellowships and training grants, as well as by the school's fundraising efforts.

"Within the first five years of our independent funding model, we've been amazed by the results," Talbot said. "The ultimate outcome of this is that we want our students to be empowered to pursue the science that means the most to them."

At the lab coat ceremony, Minor discussed the importance of the philanthropic funding for the new class.

"If you're really passionate about something, if it captures your mind, your heart and your soul, then you're going to have an impact in that area," he said. "I hope these investments give you the confidence you need to take risks right now and to persist in your explorations." ISM

GEORGE NIKITIN

Lloyd Minor addresses new doctoral students at a ceremony where they were presented with lab coats.

Sociability

continued from page 1

the reward system is so critical, it's been carefully conserved over evolution and in many respects operates just the same way in mice as it does in humans, making mice good experimental models for studying it.

Far and away the most important component of the brain's reward circuitry, Malenka said, is a nerve tract that runs from a structure deep in the brain called the ventral tegmental area to a midbrain structure called the nucleus accumbens. The ventral tegmental area houses a cluster of nerve cells, or neurons, whose projections to the nucleus accumbens secrete a substance called dopamine, altering neuronal activity in this region. Dopamine release in the nucleus accumbens can produce a wave of pleasure, telling the brain that the event going on is helpful for survival. Dopamine release in this region, and subsequent changes in activity there and in downstream neurons, also primes the brain to remember the events and the behaviors leading up to the chemical's release.

This tract, so famous for reinforcing survival-enhancing behaviors such as eating, drinking and mating, has been infamously implicated in our vulnerability to drug addiction — a survival-threatening outcome resulting from drugs' ability to inappropriately stimulate dopamine secretion in the tract. But understanding exactly how and under what natural conditions the firing of its dopamine-secreting nerves gets tripped off is a work in progress.

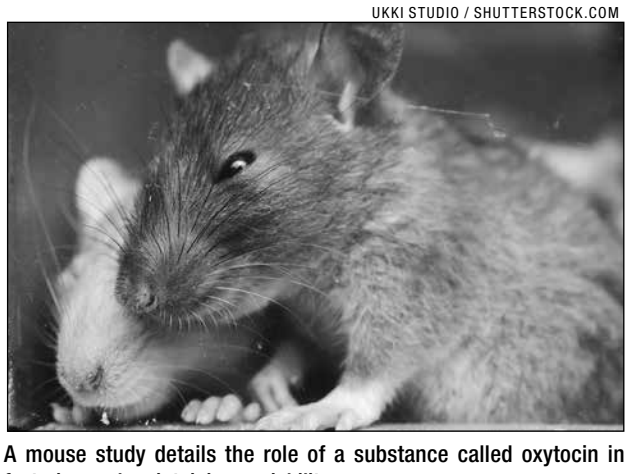
Earlier work has specifically implicated dopamine release in the nucleus accumbens in social behavior. "So, we knew reward circuitry plays a role in social interactions," Malenka said. "What we still didn't know — but now we do — was: How does this increased dopamine release during social interaction come about?"

'Love hormone' pulls the strings

It turns out that another chemical — oxytocin — is pulling the strings.

Oxytocin is sometimes called the "love hormone" because it's thought to be involved in falling in love, mother-child bonding and sexual arousal in females, as well as lifetime pair-bonding of sexual mates among some species. The chief source of oxytocin in the brain is the paraventricular nucleus, which resides in a deep-brain structure called the hypothalamus that serves as a manifold master regulator of body temperature, hunger, thirst, sleep, emotional reactions and more.

UKKI STUDIO / SHUTTERSTOCK.COM



A mouse study details the role of a substance called oxytocin in fostering and maintaining sociability.

Research over the last 20 to 40 years has suggested that oxytocin plays a role in promoting not just sexual or nurturing behavior, but also sociability. A 2013 study co-authored by Malenka showed that oxytocin was essential to reinforcing friendly, social behavior in mice. But how that occurred was unclear, as the paraventricular nucleus sends oxytocin-squirting nerve tracts to many areas throughout the brain.

So Malenka and his colleagues designed experiments to nail down oxytocin's role in social behavior. They confirmed that a tract running from the paraventricular nucleus to the ventral tegmental area carried oxytocin. They showed, for the first time, that activity in this tract's oxytocin-secreting neurons jumped during mice's social interactions and that this neuronal activity was required for their normal social behavior. Disrupting this activity inhibited sociability but didn't impair the mice's movement or their appetite for pleasurable drugs, such as cocaine.

The researchers demonstrated that oxytocin secreted in the ventral tegmental area by neurons originating in the paraventricular nucleus fosters sociability by binding to receptors on the dopamine-secreting neurons that compose the tract running from the ventral tegmental area to the nucleus accumbens, enhancing the firing of the reward-circuit tract.

The findings should help translational researchers develop medications for individuals with neurological disorders, such as autism, depression and schizophrenia, whose conditions compromise their ability to experience pleasure from connecting with other people, Malenka said.

But he also voiced a desire for more widespread applications of the research. "With so much hatred and anger in the world," he said, "what could possibly be more important than understanding the mechanisms in the brain that make us want to be friendly with other people?"

Malenka is deputy director of the Stanford Neurosciences Institute and a member of Stanford Bio-X, an interdisciplinary biosciences institute.

Other Stanford co-authors of the paper are postdoctoral scholars Jai Polepalli, PhD, and Jessica Walsh, PhD; former postdoctoral scholar Gul Dolen, MD, PhD; visiting medical student Sophie Neuner, now back in Germany; Keven Beier, PhD, instructor of psychiatry and behavioral sciences; Matthew Wright, MD, PhD, instructor of general psychiatry and psychology; Karl Deisseroth, MD, PhD, professor of bioengineering and of psychiatry and behavior sciences; and Liqun Luo, PhD, professor of biology.

The study was funded by the Simons Foundation Autism Research Initiative, the Harwell Foundation, the Kinship Foundation and the Klingenstein-Simons Foundation.

Stanford's Department of Psychiatry and Behavioral Sciences also supported the work. ISM

Opioids

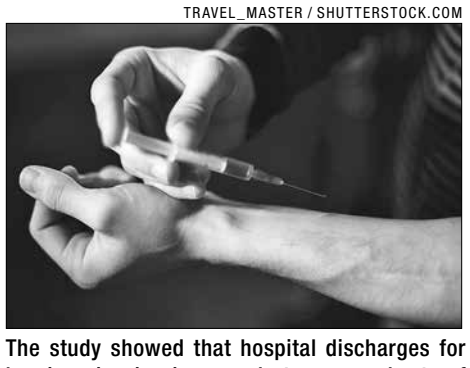
continued from page 1

analyzed national trends in hospital inpatient and emergency department discharges for opioid abuse, dependence and poisoning from 1997 to 2014, using data from the Healthcare Cost and Utilization Project, a hospital care database.

Decline since 2010

From 2010 to 2014 — the last year that data were available — researchers found a significant decrease in hospital admissions for prescription opioid overdoses, which coincided with national public health efforts to reduce the availability of these drugs, Hernandez-Boussard said.

TRAVEL_MASTER / SHUTTERSTOCK.COM



The study showed that hospital discharges for heroin poisoning increased at an annual rate of 31.4 percent from 2008 to 2014.

"While there has been a significant increase in opioid-related admissions over the past two decades, in 2010 admissions for prescription opioid misuse began to decline," she said.

In 2010, following President Barack Obama's release of the first National Drug Control Strategy, which emphasized the need for action to battle opioid misuse, addiction and overdose deaths, there were a lot of federal, national and societal initiatives targeting reductions in opioid prescriptions, she said.

"That's the good news. The bad news is that although prescription opioid use decreased, heroin and methadone greatly increased," Hernandez-Boussard said.

She added, "I'm cautiously optimistic that prescribing clinicians are positively reacting to the opioid crisis and therefore prescription opioids are contributing less to the overall drug epidemic."

Anna Lembke, associate professor of psychiatry at Stanford and author of *Drug Dealer, MD: How Doctors Were Duped, Patients Got Hooked, and Why It's So Hard to Stop*, said she has no doubt many of those addicted to prescription opioids have switched to using heroin or synthetic opioids like fentanyl.

"My patients have told me that's exactly what they did," Lembke said. "Heroin was cheaper and easier to get."

> "In the last decade, opioid-related death rates have nearly tripled."

Lembke, who did not work on this study, also said she is cautiously optimistic that the tide may be turning in terms of prescription opioids, but "there is still a long way to go, and doctors are still prescribing way too many opioids — four times as many as in the 1990s and far more than other developed countries in the world."

Among the study's limitations were the subjective nature of medical-coding practices, which can vary depending on a clinician's level of training in spotting drug abuse, and the fact that not all overdose patients make it to hospital emergency rooms, the study said.

"It is likely that many persons died of opioid misuse prior to arrival at the hospital or emergency department and would therefore not be included in our dataset," the study said.

Other Stanford co-authors of the study are Steven Asch, MD, professor of primary care and population health; Catherine Curtin, MD, associate professor of surgery; Jennifer Ha, MD, instructor of anesthesiology; and Kathryn McDonald, PhD, executive director of Stanford Health Policy.

A researcher at the University of Bologna contributed to this report.

The project was supported by the Agency for Healthcare Research and Quality.

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

Seven faculty members appointed to endowed professorships

ROBERT COWAN, MD, clinical professor of neurology and neurological sciences, was appointed the Betty Higgins Family Foundation Director, effective April 24. He directs the Stanford Headache Program. His interests include patient education, patient-provider communication and chronic daily headaches.

This position was established by Betty Higgins and her daughter, Patricia Higgins. Betty is president of the Wings of Freedom Foundation and Patricia is the founder and trustee of the Wintercreek Foundation. The directorship was created to support headache research and treatment.

CHRISTOPHER GARDNER, PhD, professor of medicine, was appointed the Rehnborg Farquhar Professor, effective June 15. His research in nutrition and diet aims to develop strategies for individuals and communities to improve their access to and consumption of healthy foods.

The professorship was established with a gift from Francesca and Carl Samuel Rehnborg and the C.F. Rehnborg Disease Prevention Fund. It was created to support research in disease prevention and honors John Farquhar, MD, a Stanford professor of medicine and of health research and policy, emeritus, who was the first holder of the C.F. Rehnborg Professorship.

KEITH HUMPHREYS, PhD, professor of psychiatry and behavioral sciences, was appointed the Esther Ting Memorial Professor, effective June 15. His research focuses on treatment and public policy affecting addiction and psychiatric disorders.

The professorship was established by George Ting, MD, and the Esther Ting Foundation Fund, which was named for his daughter who died at age 18 due to complications from addiction. It is intended to support efforts to increase understanding and treatment of addiction, particularly among adolescents.

DENNIS LUND, MD, professor of surgery, was appointed the Elizabeth Wood Dunlevie Professor, effective June 15. He is the associate dean of the faculty for pediatrics and obstetrics and the chief medical officer at Lucile Packard Children's Hospital Stanford.

The professorship was established by Bruce Wall Dunlevie in honor of his wife, Elizabeth Wood Dunlevie. Elizabeth, a board member of Packard Children's, is a longtime supporter of children's health. The professorship is intended for a faculty member serving in a leadership position in pediatric clinical affairs at the hospital.

ANTHONY ORO, MD, PhD, professor of dermatology, was appointed the Eugene and Gloria Bauer Professor of Dermatology, effective June 15. His research uses stem cells to understand tumor evolution and tissue regeneration, and his clinical interests include genetic skin diseases, hair biology and nonmelanoma skin cancer. He is the associate director of the Center for Definitive and Curative Medicine and co-director of the Child Health Research Institute.

The professorship was established with funds from anonymous donors to the Lucile Packard Foundation for Children's Health, the Stanford Medical Center Development's Biomedical Innovation Initiative and a gift from Eugene Bauer, MD, the former dean of the School of Medicine and former chair of dermatology. The position was created to support many of the translational medicine efforts that Bauer began.

BALI PULENDRAN, PhD, professor of pathology and of microbiology and immunology, was appointed the Violetta L. Horton Professor, effective June 15. His research focuses on understanding how the immune system senses microbes and viruses and then programming immune responses against them as part of the effort to design vaccines.

The professorship was created to support a faculty member whose research examines poliomyelitis or similar viral diseases. Violetta L. Horton lived in La Jolla and died in 1958.

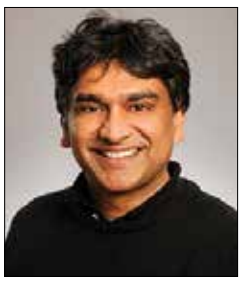
Robert Cowan

Christopher Gardner

Keith Humphreys

Dennis Lund

Anthony Oro



Bali Pulendran

LESLEE SUBAK, MD, professor and chair of obstetrics and gynecology, was appointed the Katharine Dexter McCormick and Stanley McCormick Memorial Professor III, effective June 15. Her research uses multidisciplinary approaches to treat incontinence in women.

Leslee Subak

The professorship is the third established using funds from a 1969 gift from Katharine Dexter McCormick in honor of her husband, Stanley, to support women who study or teach medicine or engage in medical research. Katharine co-founded the League of Women Voters in 1919 and contributed to the efforts to develop an oral contraceptive for women. **ISM**

OF NOTE

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

YAIR BLUMENFELD, MD, was promoted to associate professor of obstetrics and gynecology, effective July 1. His work focuses on prenatal diagnosis, genetics and clinical obstetrics. He also serves as director of fetal therapy at Lucile Packard Children's Hospital Stanford.

DIMITRE HRISTOV, PhD, was promoted to associate professor of radiation oncology, effective Aug. 1. His research interests include the development and integration of X-ray, MRI and ultrasound imaging technologies for radiation therapy guidance; improvement of radiation therapy delivery; and treatment-planning optimization and modeling.

ANNA LEMBKE, MD, was promoted to associate professor of psychiatry and behavioral sciences, effective July 1. She is medical director of addiction medicine, program director for the Stanford University Addiction Medicine Fellowship, and chief of the Stanford Addiction Medicine Dual Diagnosis Clinic.

CLAUDE NAGAMINE, DVM, PhD, was promoted to associate professor of comparative medicine, effective Oct. 1. His research focuses on using mouse models to study human infectious diseases, including dengue virus, Zika virus, coxsackievirus and anaplasma.

HEATHER WAKELEE, MD, was promoted to professor of medicine, effective Aug. 1. She specializes in the treatment of lung cancer, thymoma and mesothelioma. She also conducts clinical trials on compounds that target mutations in lung cancer and on immunotherapies for lung cancer. She is the faculty director of the Stanford Cancer Clinical Trials Office. **ISM**

Yair Blumenfeld

Dimitre Hristov

Anna Lembke

Claude Nagamine

Heather Wakelee

Matthew Porteus awarded grant for work on possible treatment for sickle cell anemia

The California Institute for Regenerative Medicine has awarded a researcher at the School of Medicine a grant of $5.2 million to lay the groundwork for a clinical trial of a possible treatment for sickle cell disease.

Matthew Porteus, MD, PhD, associate professor of pediatrics, has shown that he can take human blood stem cells with the gene defect that causes sickle cell disease and use gene-editing tools to repair the faulty gene. He also showed that he could successfully transplant those repaired blood stem cells into mice.

"We are extremely excited that, with CIRM support, we may be able to use gene correction to treat this terrible disease," Porteus said.

LUCILE PACKARD FOUNDATION FOR CHILDREN'S HEALTH

Matthew Porteus has shown that he can take human blood stem cells with the gene defect that causes sickle cell disease and use gene-editing tools to repair the faulty gene.

Sickle cell disease damages tissues, causes pain and suffering and can even be life-threatening. It is caused by a single mutation in a gene that is the blueprint for one of the proteins in hemoglobin, the molecule that carries oxygen in red blood cells. Under certain conditions, red blood cells with the sickle cell defect will change from a soft, rounded form to a rigid, sickle shape. This change makes red blood cells clump together, clogging arteries and causing organ damage. There is currently no cure for the disease, and medical treatments are mostly restricted to efforts to limit the damage it can cause.

Porteus and his colleagues are preparing to conduct a clinical trial of the technique in patients with the disease. In such a trial, clinicians would draw participants' blood, separate out their stem cells and then use a gene-editing tool called CRISPR to fix the sickle cell defect. After this, patients would be given a chemotherapy regimen that would kill off some of the patient's defective stem cells, creating places in the bone marrow where the corrected blood stem cells could take up residence when they are given back to the patient. If the treatment worked, the repaired stem cells could possibly create enough normal red blood cells for the patient to be symptom-free for life.

The interdisciplinary team at Stanford, which includes people from the new Stem Cell and Gene Therapy Clinical Trials Office and the Laboratory of Cell and Gene Medicine, is excited to be part of what may be the first instance in which a stem cell correction strategy will be given to participants in a clinical trial, Porteus said.

The grant from CIRM will be used to do the work necessary before asking the Food and Drug Administration to give the treatment the status of an investigational new drug, Porteus said. Getting this status is one of the last regulatory hurdles before a clinical trial can be put together. **ISM**