New graduate students suit up for the future

By Tracie White

The School of Medicine set recruitment records with its third-largest 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.

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

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 your friends? Why are some people so sociable while others are loners or seemingly outright allergic to interactions with others?

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 neurons that activate 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 neurons that activate when you run into an old friend or meet somebody you like.

Robert Malenka

By Tracie White

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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INSIDE STANFORD MEDICINE

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Tina Hernandez-Boussard

Robert Malenka

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

Page 5
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 the policies and practices through strategic partnerships with policymakers, philanthropists and leaders committed to fighting poverty.

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 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 SEIPEP 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 systematic, in-depth research on 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 informing and supporting them as they seek answers and solutions. Through fellowships and mentorship, 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 Jasper Sorenson, 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.

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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 future 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.

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 are being 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 intervention 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 do better? What’s the future ideal like?’" he asked.

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 non-adherent stickers. "What happens here at Stanford has the potential to shape the world!" one bright green sticky note read.

Other 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 motivators—attending open houses, learning they were supporting the Health Improvement Program, and that the plan will enhance Stanford Medicine’s focus on prevention and outcomes.

Dale Beatty, DNP, the chief nursing officer at Stanford Health Care, said he attended the event to learn more about the universitywide strategic planning efforts. "Traditional approaches to hospitalization, required an invasive procedure or led to at least three outpatient visits. Over 90% of events that led to legal action were reported that allegedly exceeded the standard of care, or that met other criteria. The protocol called for compensation to be proactively offered whenever a violation of the standard of care was caused by negligence, with 99.5 percent of cases meet these criteria. The largest payment made was $2 million. In 181 events, mostly events for which compensation criteria weren’t met, hospitals offered to wave 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 adverse events — as well as provide a specific resolution 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 CAREs investigation included new labeling for high-risk medications, color-coded socks for patients at risk for falls, radio frequency identification tags for surgical sponges, improved interpretation services, improved communication between order writers and nurses 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.
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 the 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.

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 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. Matt and Kristen Wilsey started a clinical research team from Stanford University piloted a novel way to accelerate research into the rare 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.

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. 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 review 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-phenotype data. They will be looking for ideas for early diagnosis and potential treatments.

“This effort will make a huge difference 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 use.”

‘This biobank is 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 jsung@stanford.edu.

KRIS NEWBY

CARLOS CHEM PHOTOGRAPHY

“This biobank is a tremendous step forward to curing NGLY1 deficiency.”

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)
**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 — specifically, the domestication of chocolate — specifically, the domestication of chocolate — specifically, the domestication of chocolate — specifically, the domestication of chocolate — specifically, the domestication of chocolate — specifically, the domestication of chocolate — specifically, the domestication of chocolate.

The scientists discussed the potential of developing a technique that could help scientists look at many different plants and animals at once, increasing the likelihood someone or 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 or something interesting and useful about its biochemistry, Bustamante said.

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

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 professor 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.

Cooke, Xie and colleagues set out to figure out what was in some ways the perfect test case for the methods Cooke was 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 budgies either had the yellow pigments or 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 MetaboChemistry Analysis Center and researchers from around the chemical and life sciences — and members of the American BudgeRagar and the Budge- gar Association of America, who provided samples and advice — Cooke cracked blue budgie’s color to a gene encoding a protein they dubbed MuPKS, for Melipontine undulatus polyketide synthase. (Melipontinae undulatus is the budgie’s binomial name.) A change to just one amino acid in MuPKS, the researchers found, stops budgies from producing yellow pigments, 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 in October 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 a 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.

“Without 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 or something interesting and useful about its biochemistry, Bustamante said.

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**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.**

**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 Princeton University, she was light on her feet and was the lead author of 11 scientific papers. But a complicated pregnancy, an illness in her family and time off to care for a newborn child delayed her prospects.

While she feared that the extended leave might end her research career, she was introduced to the 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 Stanford, 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.

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.

**Stanford staffer jumps back into research with help of NIH grant**

AIMEE WANG

Working with Stanford ChEM-H’s 1-year-old MetaboChemistry Analysis Center and researchers from around the chemical and life science fields — and members of the American BudgeRagar and the BudgeRagar Association of America, who provided samples and advice — Cooke cracked blue budgie’s color to a gene encoding a protein they dubbed MuPKS, for Melipontine undulatus polyketide synthase. (Melipontinae undulatus 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.

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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.
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 behavior or [redacted] 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 this year’s NIH’s High-Risk, High-Reward Research program. This year’s awards total $263 million.

Three of the Stanford scientists received Pioneer Awards, one a New Innovator Award and another 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, dispersed over five years, to investigators at all career levels to pursue new research projects that accelerate the translation of medical discoveries and develop groundbreaking, high-impact approaches to a broad area of biomedically or behaviorally relevant 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 fluororescent imaging technique that can produce images of blood vessels in the hind limbs and brains of living mice with micrometer resolution in a near-infrared regime. This technique works by injecting a dye into the animal’s bloodstream that fluorescence near-infrared light beyond 1,000 nanometers.

Dai plans to use the cash grant to push the imaging technique further toward the infrared regime, which would result in even brighter images that can be produced from greater depths within tissues. With this enhanced capability, researchers may be able to use this imaging tool to improve in-vivo 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 treatments. His overarching goal is to determine the diagnosis and treatment of various psychiatric ailments through neurobiology.

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 on 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 investor 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 community of microbes that populate 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.”

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. 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 more 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.

As a member of Stanford Bio-X and of Stanford ChEM-H, and co-director of the medical school’s Center for Human Microbiome Studies, Sonnenburg received his award for conducting fundamental, innovative research by investigators who are within 10 years of their final degree and who have not yet received a research grant or equivalent from NIH.

Lingyin Li focuses on understanding how the innate immune system works and how to harness that system for fighting 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. “The money will allow us to recruit additional postdoctoral fellows and undergraduates in this area. This will enable us to pursue the remaining mechanistic studies.”

Lingyin Li received her award to conduct fundamental, innovative research by investigators who are within 10 years of their final degree and who have not yet received a research grant or equivalent from NIH.

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

Justin Sonnenburg is a member of Stanford Bio-X, the Stanford Biophysics Program, the Stanford Neurosciences Institute, the Stanford Cancer Institute and the Stanford Neurosciences Institute.

Lingyin Li 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

These awards provide promising young scholars with financial support, training and mentoring to help them initiate their early-career research that accelerates the translation of medical discoveries into better health.

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 the Stanford Institute for Clinical and Translational Research and Education. Both programs provide promising young scholars with financial support, training and mentoring to help them initiate their early-career 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:

• mossdr
• two
dr
• five

KL2 program participants are:

• Brian Bourisuous, student, biomedical engineering and medicine
• Andrew Chang, MD, instructor, general medical disciplines
• Jack Ching, PhD student, health research and policy
• Nathan Inigo, MD, resident, vascular surgery
• Sheldon Leong, MD, fellow, nephrology and transplant

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

Information on all of the programs is available on the Spectrum website at http://med.stanford.edu/spectrum/b2/education/b3_2_research_training_program.html.
31.4 percent from 2008 to 2014.

Heroin poisoning increased at an annual rate of

We knew reward circuitry plays a role in social interaction and in downstream neurons, also primes the brain to

Drug addiction — a survival-threatening outcome re-

The ventral tegmental area to a midbrain structure called

brain’s reward circuitry, Malenka said, is a nerve tract

The ultimate outcome of this is that we want our students to be empowered to pursue the science that means the

While there has been a significant in-

They showed, for the first time, that activity in this

A mouse study details the role of a substance called oxytocin in

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

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.

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

During the 1990s, 10-20 percent of those addicted to prescription opioids were contributing less

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

The project was supported by the Agency for Healthcare Research and Quality. Stanford’s Department of Medicine also supported the work.

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

the subjective nature of medical-coding practices, which can vary depending on a clinician’s level of training in sport ing drug abuse, and the fact that not all overdose patients make it to hospital emergen cy 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 in-

The project was supported by the Agency for Healthcare Research and Quality. Stanford’s Department of Medicine also supported the work.

of the doctoral-program applicants of-
Seven faculty members appointed to endowed professorships

ROBERT COWAN, MD, clinical professor of neurology and neurological sciences, was appointed the Betty Higgin’s Family Foundation Director, effective April 24. He directs the Stanford Headache Program. His research interests include patient care, 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 GARDENER, PhD, professor of medicine, was appointed the Ruhemn Fanqahar 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 Francesc and Carl Samuel Ruhemn and the C.F. Rehnburg Disease Prevention Fund. It was created to support research in disease prevention and honors John Fanqahar, MD, a Stanford professor of medicine and of health research and policy, emeritus, who was the first holder of the C.F. Rehnburg Professorship.

KEITH HUMPHREYS, PhD, professor of psychiatry and behavioral sciences, was appointed the Elizabeth Wood Dunlevie 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 established in honor of his wife, Elizabeth Wood Dunlevie. Elizabeth, a board member of Packard Children’s, is a long-time 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 ORR, 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 non-melanoma 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 Board’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 efforts that Bauer began.

BALI PUEDNDRAN, 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 microbial stressors 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.

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

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.

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.

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 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.