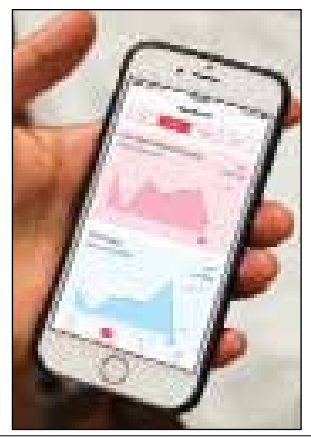
INSIDE STANFORD MEDICINE

Volume 8, No. 17 ■ September 26, 2016 ■ Published by the Office of Communication & Public Affairs



Researchers have developed an iPhone app to study peripheral artery disease.

Page 4

$600 million health research effort launches

Chan Zuckerberg Initiative funds collaboration between Stanford, UCSF, UC-Berkeley

By Amy Adams

TYLER MALLORY

Stephen Quake (left) and Joseph DeRisi walk through Quake's laboratory at Stanford. The two scientists will be co-directors of the Chan Zuckerberg Biohub.

Stanford will be one of three Bay Area universities — along with the University of California-San Francisco and the University of California-Berkeley — to participate in a new bioscience collaboration funded through a $600 million commitment by the Chan Zuckerberg Initiative.

Facebook founder Mark Zuckerberg and his wife Priscilla Chan, MD, created the Chan Zuckerberg Initiative after the birth of their daughter in 2015. On Sept. 21, the Initiative announced plans for a broader focus on science, its second major initiative, alongside work to improve education for all students. The Chan Zuckerberg Initiative's goal is to cure, prevent or manage all diseases by the end of the century by accelerating basic science research. The Initiative seeks to support new ways of enabling scientists and engineers to work together to build new tools that will empower the whole scientific community and advance progress.

The new Bay Area research collaboration, called the Chan Zuckerberg Biohub, is the first scientific investment by the Chan Zuckerberg Initiative. It will include a combination of grants, research space focused on biotechnology-tool development, and large-scale collaborative projects.

"The Biohub will be the sinew that ties together these three institutions in the Bay Area like never before," said Stephen Quake, PhD, Stanford professor of bioengineering and of applied physics, who will co-lead the Biohub with Joseph DeRisi, PhD, professor and chair of biochemistry and biophysics at UCSF.

Collaborative approach to research

The Biohub will be an independent research organization with two locations, a headquarters in the San Francisco Mission Bay district and an outstation at Stanford known as the Stanford Biohub. These hubs will establish shared biotechnology platforms and make them available to members of the collaborating universities.

"This initiative will dramatically improve our ability to conduct fundamental research at the intersection of biology and engineering that can lead to important applications for human health," said Stanford President Marc Tessier-Lavigne, PhD, who is a neuroscientist. "We are grateful for the investment by Mark and Priscilla in both sophisticated tools and an unprecedented Bay Area-wide university collaboration that will enable groundbreaking discovery."

Former Stanford President John Hennessy, PhD, was instrumental in helping establish the initiative, working closely with the Chan Zuckerberg Initiative on its inception. He will serve on the board in his personal capacity as a scientist and technologist.

"The vision for the Chan Zuckerberg Initiative and the Biohub capitalizes on the strengths of our Bay Area universities, and also makes a major investment in early-stage research of the type that cannot be readily funded elsewhere," Hennessy said. "It is large-scale collaboration at its best, and with tremendous promise for solving the world's greatest health challenges."

Resident Biohub scientists will work on two large-scale overarching projects: The Cell Atlas, a comprehensive data set cataloging all the biologically significant characteristics of every cell type in the body, and an Infectious Disease Project, devoted to tackling microbial diseases, including emerging biothreats and pandemics.

Technology to improve health

Each of the three partner schools has a long history of developing biomedical technologies, with combined strengths in medicine, engineering and the basic sciences. New opportunities created by the Biohub will focus the universities' individual strengths around the common goal of developing technologies to cure and prevent human disease, said Tessier-Lavigne.

See BIOHUB, page 6

Leadership reflects on Stanford Medicine accomplishments, looks to the future

By Kathy Zonana

Calling it "a time for us to come together and reflect on where we are today and the exciting opportunities that we have moving forward," School of Medicine Dean Lloyd Minor, MD, kicked off the first State of Stanford Medicine event on Sept. 22 before an overflow crowd of faculty, staff and students.

The event at the Li Ka Shing Center for Learning and Knowledge included an address by the dean followed by a panel discussion with David Entwistle, president and CEO of Stanford Health Care; Christopher Dawes, president and CEO of Lucile Packard Children's Hospital Stanford and Stanford Children's Health; and Minor. Megan Mahoney, MD, a clinical associate professor of medicine, moderated the panel.

Accomplishments of the past year

Standing in front of a screen listing several of the past year's accomplishments in research, education and teaching, Minor quipped, "This slide is already out of date, and we just made it yesterday." The number of faculty who had won major international awards had grown by one overnight, with assistant professor of bioengineering Manu Prakash, PhD, being named the recipient of a MacArthur Foundation "genius grant."

Among the year's

See STANFORD MEDICINE, page 6

Iron nanoparticles make immune cells attack cancer, according to new study

By Erin Digitale

Iron nanoparticles can activate the immune system to attack cancer cells, according to a study led by researchers at the School of Medicine.

The nanoparticles, which are commercially available as the injectable iron supplement ferumoxytol, are approved by the Food and Drug Administration to treat iron deficiency anemia.

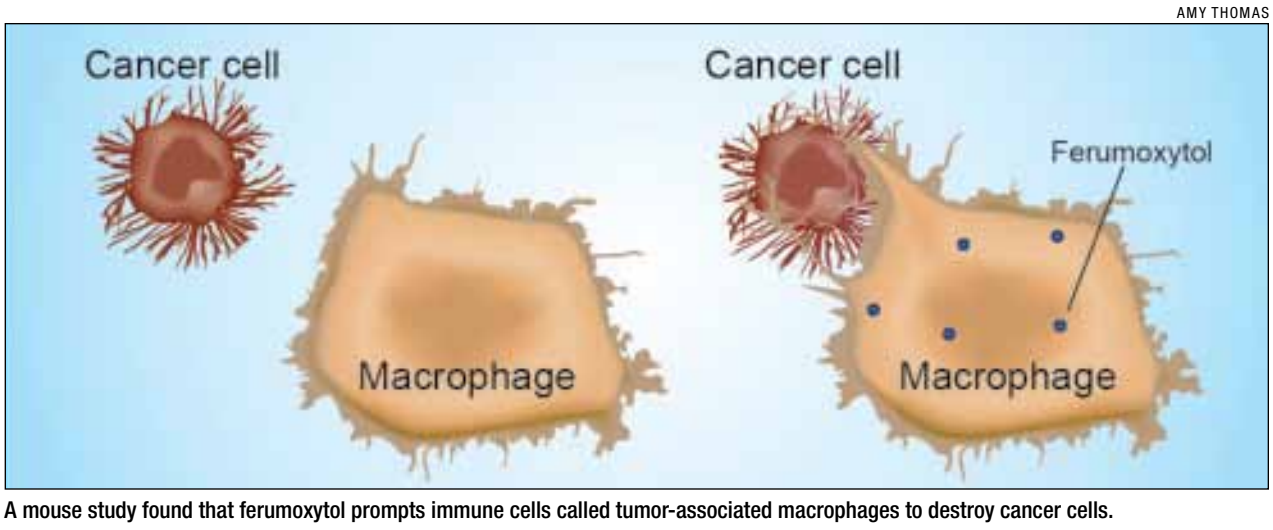
The mouse study found that ferumoxytol prompts immune cells called tumor-associated macrophages to destroy cancer cells, suggesting that the nanoparticles could complement existing cancer treatments. The discovery, described in a paper published online today in *Nature Nanotechnology*, was made by accident while testing whether the nanoparticles could serve as Trojan horses by sneaking chemotherapy into tumors in mice.

"It was really surprising to us that the nanoparticles activated macrophages so that they started to attack cancer cells in mice," said Heike Daldrup-Link, MD, who is the study's senior author and an associate professor of radiology at the School of Medicine. "We think this concept should hold in human patients, too."

Daldrup-Link's team

See IRON, page 6

AMY THOMAS



A mouse study found that ferumoxytol prompts immune cells called tumor-associated macrophages to destroy cancer cells.

School's Grant Writing Academy honored with AAMC award

By Becky Bach

Success as a professional scientist is increasingly determined by the ability to secure funding. Yet grant writing — the nitty-gritty work of distilling ideas into a winning pitch — is rarely taught in graduate school or postdoctoral training.

Recognizing this gap, Stanford Biosciences launched the Grant Writing Academy in 2014. Though young, the program has already boosted the number of both grant submissions and funded grants, said its director, Crystal Botham, PhD. It recently earned national recognition as well: It was honored as the third-prize winner of the Association of American Medical Colleges' Innovations in Research Education Award.

Though the program specializes in helping students and postdoctoral scholars write some of the most common grants offered by the National Institutes of Health and the National Science Foundation, they are welcome to use it to apply for any bioscience grant, Botham said.

NORBERT VON DER GROEBEN

Lamia Wahba, a postdoctoral scholar in pathology, coaches participants in a workshop offered through the Grant Writing Academy.

Proposal boot camp

Chandramouli Chandrasekaran, PhD, a postdoctoral scholar in neurosciences and electrical engineering, turned to the Grant Writing Academy for assistance applying for a NIH Pathway to Independence Award from the National Institute of Neurological Disorders and Stroke. The grant can provide up to five years of funding, but it demands as many as 30 documents that need to be nearly perfect, Chandrasekaran said. That seemed a bit overwhelming, so he attended the academy's proposal boot camp, a two-month course that meets weekly and walks a cohort of graduate students and postdocs through each step of the grant-application process.

The boot camp helped Chandrasekaran, who studies the neural mechanisms underlying decision-making in primates, secure one of the coveted awards. Now, he recommends it highly.

"It helped demystify many aspects of the process for me, and it gave me a huge boost in self-confidence," he said. "I was able to become good friends with another person in my class at the academy, and in the days before the deadline we helped each other as proofreaders."

So far, the academy has worked with about 180 students and trainees, Botham said. She attributes its success, in part, to its use of peer mentors. "Peer feedback is really valued. There's only one of me, and I can't read 100 grants, but I can train grant coaches to work with 100 postdocs or graduate students," she said.

Lamia Wahba, PhD, a postdoctoral scholar in pathology, is one of the academy's grant coaches. She said the academy has helped her refine her own grants, but it has also taught her a lot about teaching. Teaching writing is quite different from teaching genetics, she said. It requires trainees to examine their research critically, she said.

'You become a better scientist'

"By being able to write and articulate your research goals, you become a better scientist," said Botham.

And some of the most common mistakes inexperienced grant writers make? Many make assumptions about what the reviewers know, Wahba said. Even experts in the field may not be familiar with new or unusual techniques, she said. In addition, beginning grant writers often struggle to keep their writing concise and to resist the temptation to include every detail, she said.

"The big take-home lesson is we weren't taught enough about writing about science," Wahba said. Oftentimes, trainees think they need to write grants in the evenings or weekends, and think of it as not part of their actual job, she said. "I really learned the importance of having it be a part of your job. This is actually work as well, and it needs to be done really well," she added.

The academy's annual proposal boot camp, which meets weekly, begins today. It runs to Nov. 17. The academy also offers periodic lectures and workshops, as well as drop-in hours with grant coaches. **ISM**

New program in physician assistant studies now accepting applications

By Tracie White

The School of Medicine will for the first time offer a master of science program designed to train physician assistants as both clinicians and future leaders in health care.

"As health-care access improves, we need to equip medical practitioners with the skills to meet growing demand," said medical school Dean Lloyd Minor, MD. "This new master of science program for physician assistants helps health-care teams navigate that complexity and provide precision health: personalized treatment when disease strikes and proactive and preventive care that keeps people from getting sick in the first place."

To be considered for admission to the program in the fall of 2017, applications are due Nov. 1.

"This program will set itself apart from many other physician assistant programs by combining excellence in clinical training with scholarly projects that will help our graduates to become future leaders in their field," said Charles Prober, MD, senior associate dean of medical education.

Designed for a class of 25 to 30 students, the 30-month program will emphasize training alongside medical students in coursework and clinical care. It will also require students to choose an area of scholarly concentration within one of four areas: community health, health services and policy research, clinical research or medical education.

> "We are trying to educate the next generation of PA leaders."

"With the increasing emphasis on coordinated, team-based care as supported by the Affordable Care Act, it is critical that the School of Medicine be able to create an integrated, team-learning environment to educate the biomedical scientists and clinicians of the future," said Robert Harrington, MD, professor and chair of medicine.

Replaces former program

The master's degree program replaces the associate degree program to train physician assistants that began in 1971 as a partnership between the School of Medicine and Foothill College, a two-year community college in Los Altos. The associate degree program will no longer be offered once its current students have graduated.

The new program is designed to meet the expanding role of PAs in today's changing health-care environment, said Susan Fernandes, PA, clinical professor of pediatrics and of medicine.

"Today's PAs practice in all areas of medicine," Fernandes said. "They are leading community health centers, they are front stage in the health-care policy arena, leaders in the classroom and changing health-care delivery through innovation and research."

The role of the PA, one of the fastest growing professions, has expanded in part due to a shortage of physicians nationwide and the need to meet the growing demands of an aging population, Fernandes said. She and Rhonda Larsen, PA, clinical assistant professor of pediatrics, worked as consultants to help design the new program.

"We are trying to educate the next generation of PA leaders," Larsen said. "No other program sets out to do this."

LISA CAVIN

Physician assistant students Liliana Camacho and Edilberto Canseco learn how to scrub into an operating room.

'New direction for Stanford'

PAs treat patients as part of a health-care team, collaborating with physicians and other providers, Fernandes said. They often provide a broad range of health-care services that may include conducting physical exams, ordering and interpreting medical tests, diagnosing illnesses, developing treatment plans, prescribing medication and assisting in surgery.

"This is a new direction for Stanford, which has been traditionally a very research-heavy medical school," said Andrew Nevins, MD, clinical associate professor of medicine and medical director of the new program. "There is little training of advanced practice providers such as PAs. There is no school of nursing, no pharmacy school. This is an opportunity for Stanford to make a mark on this rapidly growing field."

The curriculum will emphasize training in the foundational sciences during the five quarters, followed by a year of clinical clerkships. There will be clerkships in obstetrics and gynecology, internal medicine, ambulatory family medicine, pediatrics, surgery, psychiatry and emergency medicine. In addition, students will have several elective rota-

See PA, page 3

INSIDE STANFORD MEDICINE

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

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

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

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

STANFORD MEDICINE

5 QUESTIONS

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

Beth Darnall on opioids and pain management

Beth Darnall, PhD, is a clinical associate professor of anesthesiology, perioperative and pain medicine at the School of Medicine. She has more than 15 years of experience as a pain psychologist treating a variety of individuals with chronic pain. For example, she has worked extensively with patients suffering from spinal cord injuries, catastrophic burns, amputations, chronic low back pain, migraines, fibromyalgia and various types of musculoskeletal pain.

Darnall is co-principal investigator for a National Institutes of Medicine-funded project that is studying treatment for pain catastrophizing, which is a distressing pattern of thoughts and emotions commonly experienced by those with chronic pain. She has also developed a novel pain psychology treatment that can be delivered over the internet to patients before surgery to help reduce distress and optimize post-surgical healing and recovery. The treatment uses meditation and cognitive behavioral therapy to help patients avoid negative thought patterns that can amplify pain. This is currently being tested in women undergoing surgery for breast cancer.

Her clinical practice, research and public-education efforts focus on empowering people with chronic pain to target their daily choices, thoughts and emotions that can worsen pain and harness the power of their mind-body connection to reduce their symptoms and increase their quality of life.

She is co-chair of the Pain Psychology Task Force at the American Academy of Pain Medicine, and is a 2015 recipient of the Presidential Commendation from the American Academy of Pain Medicine.

Stanford Health Care writer Jana Chow recently spoke with Darnall about pain management and her newly released book, The Opioid-Free Pain Relief Kit*, which includes tools to equip patients to manage pain. The book includes a relaxation CD that is designed to calm the nervous system. Darnall is also the author of* Less Pain, Fewer Pills: Avoid the Dangers of Prescription Opioids and Gain Control Over Chronic Pain*, which was published in 2014.*

1 What are the best tools you've found to reduce pain without opioids?

DARNALL: While the term "painkiller" is common, it's a misnomer when applied to opioids for chronic pain. Studies show that when used long-term, on average, opioids only reduce pain by about 25-30 percent. It's critical that other strategies be used by patients to gain relief. Brain-training therapies, such as cognitive-behavioral therapy, mindfulness-based stress reduction, and meditation have similar pain-relieving effects, with none of the side effects. By learning techniques that reduce attention to pain — and distress about pain — pain is relieved. It's not just about teaching patients how to cope with their pain — the techniques actually reduce pain processing in the nervous system, thereby directly reducing its intensity and impact. Think of it as mind-body medicine.

IAN MACKEY

Beth Darnall is the author of a new book on pain management.

Learning how to calm one's own nervous system is a critical aspect of pain management. It's vitally important to learn and use skills to control the cognitive, emotional and physiological factors that amplify pain. Even if opioids are prescribed, they should be just one part of an overall, comprehensive pain care plan that includes pain psychology, self-management, movement therapy or appropriate exercise, and other disciplines.

By learning to calm the nervous system, people can gain confidence in their ability to manage their own pain and related distress. We call this confidence "self-efficacy," and it's a powerful predictor for whether people will get better or not. People who believe they have tools to reduce their distress and suffering are more likely to use those skills, and gain good results from them. Part of our job as pain psychologists and health-care providers in general is to help connect patients to the right information so they can employ strategies and techniques to self-manage their symptoms.

2 What happens when patients taper off of opioids? Does their pain increase or decrease?

DARNALL: Many people remain on opioids out of fear that their pain will increase if they stop taking them. However, the data show that when people taper off opioids slowly, their pain tends to remain the same or improve. If opioids are stopped too quickly or if a single dose is missed, withdrawal symptoms are likely to occur, along with worse pain. A good, slow opioid taper will help patients avoid withdrawals altogether.

3 How can medical schools better equip physicians to treat pain without medication?

DARNALL: Most medical schools do not prepare physicians to handle the complexities of chronic pain management. A 2011 study showed that most U.S. medical schools included only four to 11 hours of specific educational content on pain across the entire four-year program — and that small amount of content was fragmented by topic. Pain was addressed within disease education — such as cancer or diabetes — instead of through a dedicated curriculum on comprehensive pain treatment. Physicians and all health-care providers need better training in the biopsychosocial model of pain treatment, and this need was identified by the 2016 National Pain Strategy developed by the U.S. Department of Health and Human Services.

Earlier this year, I, along with my colleagues on the Pain Psychology Task Force at the American Academy of Pain Medicine, published results from a national needs assessment we conducted about pain psychology training and resources. We surveyed 2,000 individuals across six key stakeholder groups in the U.S. Our results showed that, similar to physicians, the majority of mental health professionals and psychologists feel inadequately trained to address pain in the therapeutic context. Consequently, therapists may avoid the topic with their patients, thereby missing a critical opportunity to help their patients better manage their pain by emphasizing evidence-based behavioral skills and techniques.

While better education on the biopsychosocial treatment model of chronic pain is needed in medical schools, we also must give physicians and health-care professionals the resources to actually implement biopsychosocial pain care. This goes back to needing better training for mental health professionals so that primary care providers can easily refer their patients to competent therapists in the community who will directly address pain as a therapeutic target. In the pain psychology national needs assessment, we identified that pain education is needed at all levels of psychology education, including undergraduate, graduate, postgraduate, to continuing education for community professionals.

4 How does the mind impact pain?

DARNALL: The mind has a tremendous influence on the experience of pain. Multiple fMRI studies show that focusing on pain or ruminating on it can cause it to worsen. Rumination is one aspect of pain catastrophizing — when a person focuses on pain, magnifies it and feels helpless. The good news is that pain catastrophizing is treatable, and this is the focus of much of my NIH research. It's an important therapeutic target because catastrophizing is linked to the development of chronic pain after surgery or an episode of acute pain. I teach my patients that even though they have a diagnosed medical condition, they are participating with their pain through their choices, thoughts and emotions. While we can't change the medical diagnosis, we can target daily choices, thoughts and emotions to gain control and change the trajectory of pain.

5 How do people with psychological distress respond differently to opioids?

DARNALL: Anxiety and depression are common in individuals with chronic pain, and these conditions serve to worsen pain. Research shows that individuals with anxiety and depression are more likely to be prescribed opioids, and at higher doses. This is problematic because opioids may be unwittingly prescribed to treat the psychiatric symptoms that feed into pain. Opioids don't just blunt physical pain, they blunt emotional experience, too, and this can be a powerful reward to an individual suffering from emotional distress related to pain or just life in general — and it can prolong opioid use. It's critical that we address psychological distress with evidence-based treatments that emphasize behavioral medicine — psychological treatment. Emotional pain serves to increase physical pain, and vice versa; it is crucial that we treat both the physical and emotional experience because this yields the best results, and it helps avoid overreliance on medication and addiction. **ISM**

PA

continued from page 2

tions that allow them to specialize in their area of interest. For example, a student interested in a career as a surgical PA can complete up to 12 weeks of clerkship in that area.

Currently there are about 150 accredited training programs nationwide for PAs, almost all master's programs, with about 70 to 80 new programs on the horizon, Larsen said.

The number of practicing PAs has grown from 14,000 in 1990 to about 100,000 today, according to the American Academy of Physician Assistants. The average salary is about $98,000 a year.

Employment of physician assistants is projected to grow 30 percent between 2014 and 2024, much faster than the average for all occupations, according to the U.S. Bureau of Labor Statistics. **ISM**

Marius Wernig, Manu Prakash named Faculty Scholars

Two School of Medicine faculty members are among 84 early-career scientists to be named 2016 Faculty Scholars by three philanthropic organizations.

The five-year grants were announced Sept. 22 by the Howard Hughes Medical Institute, the Simons Foundation and the Bill & Melinda Gates Foundation. The three organizations will spend about $83 million over the course of the grant period to support the recipients. The total award for each researcher ranges from $600,000 and $1.8 million, including indirect costs. The two grant recipients from the School of Medicine are Manu Prakash, PhD, assistant professor of bioengineering, and Marius Wernig, MD, PhD, associate professor of pathology.

Prakash was named an HHMI-Gates Faculty Scholar. He studies simple animals to better understand how a small collection of cells gives rise to a multicellular organism. He also develops new imaging tools and techniques based on soft-matter physics that aid in his quest to understand the origins of complex behavior in simple animals. In addition, he develops tools for "frugal science" — inexpensive devices that can be used to tackle global health problems and that also aim to democratize access to scientific experience.

Wernig was named an HHMI Faculty Scholar. He investigates the molecular mechanisms that determine cell lineage identity, focusing on reprogramming skin and stem cells into functional neurons. His work includes translational efforts to treat an incurable genetic skin disease and various diseases of the nervous system, such as multiple sclerosis.

Three other Stanford faculty members also received grants. They are Alex Dunn, PhD, associate professor of chemical engineering, who was named an HHMI Faculty Scholar; Elizabeth Sattely, PhD, assistant professor of chemical engineering, who was named an HHMI-Simons Faculty Scholar; and Jan Skotheim, PhD, associate professor of biology, who was named an HHMI-Simons Faculty Scholar.

Manu Prakash

Marius Wernig

This is the first collaboration between the philanthropies, which created the Faculty Scholars program in response to growing concern about the significant challenges that early-career scientists face. Researchers with more than four, but no more than 10, years of experience as faculty members were eligible to receive grants. More than 1,400 scientists from 220 institutions applied for them. **ISM**

IPhone app launched to study peripheral artery disease

NORBERT VON DER GROEBEN

Oliver Aalami (second from left) walks with members of his team that helped develop the app. They are Raheel Ata (far left), Neil Gandhi (second from right) and Sunaina Kongara (far right).

By Tracie White

School of Medicine researchers have launched a free iPhone app designed to help them conduct a clinical study to discover better treatments for peripheral artery disease and as a convenient way for people with the disease to monitor their daily activity.

"We hope to gain insights into patterns of disease progression over time by collecting participants' activity data from their iPhones," said Oliver Aalami, MD, clinical associate professor of vascular surgery and lead investigator of the study. "We will be looking for any changes in activity patterns that may indicate disease advancement."

Peripheral artery disease, which affects about 12 million people in the United States, is a circulatory problem caused by a buildup of plaque in the peripheral arteries, most commonly in the legs. Symptoms include cramping and pain while walking or climbing stairs. Treatment is directed at reducing leg pain and the risk of heart attack and stroke from clogged arteries.

'It gets really painful'

"One of the key metrics we will look at is the greatest distance that people with PAD can walk without stopping," Aalami said. "It gets really painful, and they have to stop and rest before continuing on."

The VascTrac app will collect activity data using Apple's ResearchKit, an open-source framework that allows iPhone users to easily join clinical research studies. Since its launch over a year ago, the software has been used by researchers to collect data on diseases ranging from diabetes to melanoma. Stanford researchers launched one of the first of these studies, MyHeart Counts, in the spring of 2015 to study heart disease. That study has enrolled more than 54,000 people so far.

NORBERT VON DER GROEBEN

The VascTrac app is designed for people who have peripheral artery disease. It tracks a user's steps and activity during the day.

Aalami said the goal for the PAD study is to enroll 2,000 to 5,000 participants, "much more than you can do with a traditional trial."

One of the study's aims is to see if people with PAD show sudden changes in activity level in the months after certain common vascular procedures, such as the use of stents and balloons to improve blood flow in the arteries. Knowing exactly when a sudden drop in activity occurs, rather than waiting for the traditional follow-up doctor's visit, could potentially provide physicians and participants with a much better indication of when further intervention is needed. A sudden drop in activity level could be a sign of claudication — pain caused by too little blood flow to the extremities, commonly the legs, which indicates trouble.

"People with PAD may be able to walk five miles, but sudden pain may cause them to stop often," Aalami said. These patients can rest, and the pain goes away and they move on, often not realizing they could be in trouble, he said.

Early detection a 'Holy Grail'

"Endovascular procedures such as balloons or stents in the iliac or femoral arteries are minimally invasive procedures that allow patients to go home the same day, and they work well, but are not that durable," Aalami said. "The issue is that within a year or two, 60 percent of them fail because patients develop scar tissue. We're not perfect at predicting who is going to have problems, and catching them early when these stents do go down would be the Holy Grail. It's much easier to fix earlier."

Traditionally, physicians tell patients to schedule follow-up visits at three-, six- and 12-month intervals after one of these procedures. But there's a "black hole" in between visits when doctors don't know what's happening, Aalami said.

The app "could be a game changer," said Neil Gandhi, a Stanford medical student and co-investigator of the study. "It could change the way physicians practice. By using personalized tracking, participants could get a notification to come in for an ultrasound when physicians see signs of claudication. This could ultimately improve care."

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

Although the app is targeting people with peripheral artery disease, any iPhone user 18 years or older is qualified to participate in the trial.

"Because anyone can develop peripheral artery disease, and because we need healthy subjects as controls, we're opening the study to anyone," said Raheel Ata, a Stanford medical student and co-investigator of the study.

Participation will include a five- to 10-minute initial survey, followed by quarterly surveys on the iPhone and occasional tests to measure how far a participant is able to walk. To keep a daily tally of activity, users simply keep their iPhone with them during the day.

"We've tried to keep participation in this trial as simple as possible," Aalami said. "The phone will passively measure total steps taken in a day, the number of stairs walked and the distance walked." Participants can download the VascTrac app from the App Store.

Researchers emphasize that the app is not a medical diagnostic tool and isn't designed to provide medical advice, professional diagnosis, opinion, treatment or health-care services.

All participants' data will be stored using military-grade encryption, and participant names will be replaced by random codes, keeping identities and medical information confidential, the researchers said. With permission from a participant, his or her de-identified data may be shared with researchers at other institutions approved by Stanford.

The trial is being sponsored by the companies Abbott Vascular, Cook Medical, W. L. Gore & Associates and Microsoft. ISM

Regulatory RNA essential to DNA damage response, study shows

By Krista Conger

Knowing when to hold them, and when to fold them, is a critical skill in professional gambling. But it's also pertinent for cells assessing DNA damage.

It's essential for the cells to quickly ascertain whether it's possible to repair mistakes or to self-destruct for the good of the organism. That's because cells with a damaged genome often begin to flaunt the standard rules of growth and become cancerous.

Now, researchers at the School of Medicine have discovered a new player in this high-stakes molecular game in the form of a novel regulatory RNA they've named DINO. This RNA molecule binds to and stabilizes a well-known tumor suppressor protein called p53 that mobilizes a cell's response to DNA damage. When mutated, p53 is one of the most infamous bad guys in the cancer world.

"It's so important for a cell to keep track of potentially dangerous changes to its genome," said professor of dermatology Howard Chang, MD, PhD. "But if cells reacted to every little ding, they would find themselves responding inappropriately — they would stop growing and maybe even self-destruct unnecessarily. You don't want to do this unless the DNA damage is severe. We've discovered that DINO is an integral part of this decision-making circuit."

A paper describing the research was published online today in *Nature Genetics*. Chang is the senior author. Lead authorship is shared by former radiation oncology resident Adam Schmitt, MD, graduate student Julia Garcia and former graduate student Tiffany Hung.

When DNA gets damaged

Howard Chang

DNA damage is a natural byproduct of cell division because it is impossible to faithfully copy each of the 3 billion nucleotides that make up our genomes without making at least a few errors. Damage can also be caused by exposure to certain chemical agents, ultraviolet light and ionizing radiation.

Most of the time these problems are recognized and quickly repaired by the cell. That's where p53 comes in. When it is doing its job, p53 recognizes and responds to DNA damage by increasing the expression of genes involved in DNA repair and cell division. In this way it functions as a tumor suppressor. When mutated, however, p53 loses its ability to modulate the cell's response to DNA damage. Mutations in p53 are among the most common causes of many types of cancer.

Chang and his collaborators found that p53 also increases the expression of DINO. DINO, in turn, binds to and stabilizes p53 in a kind of positive feedback loop, amplifying its signal throughout the nucleus.

"Until now, most studies have focused only on proteins in this pathway," said Chang.

Fine-tuning the damage response

DINO is a member of a group of RNA molecules known as long noncoding RNAs, or lncRNAs. These molecules have been implicated in a growing number of critical regulatory roles throughout the cell. This is the first time that a lncRNA has been shown to be involved in this critical DNA damage-response pathway in living animals.

Chang and his colleagues found that when DINO expression is artificially increased, cells respond as if their DNA has been damaged even in the absence of any genome changes. In contrast, when DINO expression is inhibited, the cell responds less robustly to signals from p53.

"DINO expression allows the cell to fine-tune its response to DNA damage and respond appropriately," said Chang.

Because, as an RNA, DINO is made in the cell's nucleus where p53 is active, the researchers believe it may provide a more rapid and precise response to DNA damage than would a regulatory protein, which would be synthesized **See RNA, page 5**

Stanford Health Care addresses needs of an aging population

By Sara Wykes

As director of Stanford Health Care's Adult Aging Services program for more than a decade, Rita Ghatak, PhD, has guided thousands of older patients and their families through the health maze that starts, at least on paper, at age 65.

Traditionally, dementia support has been one of the program's most sought services. But today, a ballooning population of older patients is asking for broader guidance on healthy aging. "People are telling us they want to plan before a crisis develops," Ghatak said. "We are expanding our programs to help them avoid last-minute scrambles — and building out our services that support the prevention of age-related problems, either for the older person or an adult child."

The need is clear: Worldwide and nationwide, the aging population is growing faster than any other cohort. California's 65-and-older population already tops 5 million. Four in 10 patients at Stanford Hospital are from that age group. It's a patient population whose care will be complex: Being 65 typically means having at least one chronic health condition that cannot be cured, but only managed. Age also greatly raises the risk of heart disease and cancer, and decreases vision, hearing, bone strength and joint mobility.

Expanding care

Stanford Health Care, in collaboration with the School of Medicine, is expanding its systemwide health care for patients 65 and older. "We have made senior care one of our priorities," said Marina Martin, MD, clinical assistant professor of medicine and and section head for geriatric medicine. "We've done programs here and there to address gaps. Now we are going to look at how we can adapt the whole SHC system to care for this increasingly large group of patients."

Care for older adults has traditionally been one-size-fits-all, Martin said, but it needs to be tailored, particularly for the oldest and frailest age group, whose health is the most precarious. The goal of SHC's new geriatrics-care effort, she said, will be to provide effective care for everyone 65 and older, no matter their health status, and to focus on preserving their quality of life. "We are designing a road map for change so that no matter where in the system an older patient lands, we will be able to deliver the best possible care," she said.

Aging Adult Services "has filled a major gap," Martin added, providing resources, special programs and training. Many of Aging Adult Services' programs are now known as national models. Its strategies include building a strong continuum of care among a patient's doctors, nurses, social workers and case managers so everyone understands what that patient wants from health care.

'They are vulnerable'

"We have a lot of older medical patients who need advice on healthy living and managing their chronic disease," said Candace Mindigo, a registered nurse and longtime Aging Adult Services care coordinator. "They are vulnerable." After a recent talk at a Palo Alto senior center, Mindigo was bombarded with questions. Some of them illustrated just how unfamiliar the health-care system can be for people with little experience navigating it. "They wanted to know," Mindigo said, "who, if you are hospitalized, do you talk to if you have questions?"

Aging Adult Services personalizes its care plans for patients and their caregivers because they face health conditions and circumstances that can vary widely. "Every person ages differently no matter what the diagnosis," said Jennie Clark, a gerontologist and manager of the service's Memory Support Program. "We focus on person-centered care. Even if a patient is functionally or physically impaired, they still have capabilities. We focus on who the person is now and how they want to live their life."

That care also includes attention to the challenges of aging beyond physical ailments, said Dolores Gallagher-Thompson, PhD, professor emerita of psychiatry and behavioral sciences. Gallagher-Thompson directs Stanford Medicine's Older Adult and Family Center, which works to improve the well-being of family caregivers of dementia patients, and collaborates with Aging Adult Services. Fear and loss, she said, can affect an older patient's emotions and behavior.

"The fear of dementia is very common," she said. "There are also lots of losses during this time — of a spouse, of friends, of function. We regularly talk with our aging patients about counting blessings and letting go of past hurts and resentments. When we work with caregivers, we try to build their resilience and to help them revitalize from the emotional exhaustion that comes with that role."

The gift of listening

The center has developed a number of innovative resources for aging adults and their families, she said, including a manual to guide therapists treating late-life depression. It is also developing a fotonovela focused on teaching Latino family caregivers how to effectively manage difficult everyday behaviors in their family members with dementia.

Terese McManis, a registered nurse and the manager of Aging Adult Services, is an expert at the delicate conversations that may be needed at this stage in life. She and her team help families talk about decisions that affect a patient's independence and self-respect: when to stop driving, when extra help at home is needed or when home health care is not enough.

"I try to get everyone on the same page," McManis said, "and remind them that they, too, are going to be in the same position one day, so remember to be patient." Sometimes, staff members will make a home visit to learn more about a patient and family's circumstances. Home visits allow them to perform clinical evaluations of how well patients are following doctors' orders and to help patients accomplish health goals.

NORBERT VON DER GROEBEN

Terese McManis, a registered nurse and the manager of Aging Adult Services, visits Cherie Helm at her home in Santa Clara.

Always, Mindigo said, Aging Adult Services acts as a sounding board. "The biggest part of what we do is to be a support, to navigate, to refer and to provide resources," she said, "but we begin by listening. That is a gift we can give to them so they can sort things out. And if any of this eases their burden of care and helps them feel connected to an advocate, it improves their overall quality of life. It starts with someone listening with respect, whether or not an illness has been diagnosed."

"You have to be a good listener," McManis said. "Everybody has a story to tell." ISM

Biodesign fellows to develop health technology for aging adults

By Sara Wykes

The Stanford Byers Center for Biodesign has joined Stanford Health Care's efforts to advance care for the aging population by selecting aging as the clinical focus for its 2016-17 Biodesign Innovation Fellows program. It was not a hard choice.

"Aging as a health issue is both an extraordinary crisis and opportunity," said Paul Yock, MD, founder and director of the center. "It's the single most interesting area for innovation we could have chosen."

It also made sense, Yock said, "because aging gives us a way to shift from just fixing disease to looking at health — what will it take to keep people happy and healthy into their later decades."

Stanford Biodesign, which celebrated its 15th anniversary this year, has trained more than 1,000 graduate students and nearly 200 fellows in the process of health technology innovation. Those trainees have gone on to found more than 40 companies and develop products that have benefited more than half a million patients.

This year, all 12 fellows will follow the program's usual process of gathering information, identifying needs and developing solutions. But because research has shown that older adults generally want to stay in their homes, the fellows will spend time with people in their homes and in transitional care facilities, in addition to their traditional clinical immersion experience at Stanford Hospital.

Collaborating with Center on Longevity

The biodesign program is collaborating with Stanford's Center on Longevity, which has given this year's fellows "a treasure trove of people and ideas," said Yock, a professor of bioengineering and of medicine.

This year's fellowship program also reflects the biodesign program's renewed emphasis on cost innovation, Yock said. "We'll be looking at areas where, as a health system, we are spending enormous resources in ways that are not intelligent, effective or caring. Those are areas where innovation is necessary."

The fellows are not told what their focus will be before they arrive at Stanford, and they have responded with great enthusiasm to working on health-care innovation for older patients. "Given the magnitude of our aging population, both in the U.S. and abroad, I am thrilled to address the needs in this area," said biodesign fellow Eric Kramer, a mechanical and biomedical engineer. "I believe that our focus on value innovation, combined with what older people can teach us, will help us find meaningful ways to improve care."

Vivien de Ruijter, MD, worked at an angel investment firm before being selected as a biodesign fellow. In conversations she had there, "the consensus was that the aging population is a global concern — and that there are broad opportunities to intervene and improve care."

Already, Kramer said, he has begun to recognize the nuances of discovering the needs of an older population. "Some people need more help, but even they wanted to keep the conversation upbeat. Finding the right way to get people to open up and tell us about things that may be less pleasant will be part of the challenge." ISM

RNA

continued from page 4

in the cytoplasm.

"Positive feedback loops are used in many applications, including engineering, to increase the sensitivity of systems and apply thresholds for action," said Chang. "We believe DINO may play role in cancer development and possibly premature aging by modulating how a cell responds to DNA damage."

Other Stanford co-authors of the paper are graduate student Ryan Flynn; bioinformatician scientists Ying Shen, PhD, and Kun Qu, PhD; former graduate student Alexander Payumo, PhD; undergraduate student Ashwin Peres-da-Silva; postdoctoral scholar Daniela Broz, PhD; professor of chemical and systems biology and of developmental biology James K. Chen, PhD; and professor of radiation oncology and of genetics Laura Attardi, PhD.

The research was funded by the National Institutes of Health, the ASCO Conquer Cancer Foundation, a Susan G. Komen Young Investigator Award and Stanford Radiation Oncology Kaplan Funds.

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

Biohub

continued from page 1

"The Biohub will provide many new opportunities for interdisciplinary collaboration," said Ann Arvin, MD, Stanford's vice provost and dean of research. "By bringing together basic biomedical scientists, engineers and clinician investigators from across the three universities, the Biohub will greatly expand the development of new technologies needed to tackle major health challenges."

Quake said the Biohub's focus on technology makes sense, given the history of technological advances that have helped scientists understand, treat and prevent disease. In his own lab, Quake developed a platform called microfluidics, which can sequence miniscule amounts of DNA or analyze molecules within drops of liquid. It has greatly accelerated research into the genetic basis of disease and underlies lifesaving biomedical assays.

DeRisi, who earned his PhD in biochemistry at Stanford, has developed genomic technologies for studying infectious disease such as malaria and viruses, and diseases of unknown origin. His technologies have identified drug targets for infectious diseases, with drug candidates now in clinical trials.

Other advances to come out of the collaborating universities include recombinant DNA, genomics platforms and CRISPR/Cas9, among many others. Combining the strengths of the universities will accelerate the pace of new, equally groundbreaking technologies.

"With this extraordinary commitment, we are closer than ever to beating disease," said Lloyd Minor, MD, dean of the School of Medicine. "These resources will support the kind of curiosity-driven basic research that has led to history's most important health advances — and the remarkably talented minds behind it."

Supporting people

The Biohub will fund Chan Zuckerberg Investigators to support high-impact projects that are too exploratory to receive government support. The competition for these slots will open to faculty at the three universities in October, and selections will be made by a panel of independent scientists probably by the end of the year, Quake and DeRisi said. The Chan Zuckerberg Initiative will not be involved in reviewing and selecting investigators.

"We're going to look for people who are doing things that will change the world," said Quake, who is also Lee Otterson Professor in the School of Engineering. The streamlined application process will be based on an outstanding idea and a record of success, with the idea that people who have done well before tend to do well again, Quake said.

Three Biohub programs focus on fostering the careers of young scientists. One is a fellowship program to support outstanding recent graduates that gives those scientists a boost to their early careers. Quake added that the fellowships will keep elite young scientists in the Bay Area ecosystem rather than losing their expertise to other universities.

The Biohub's scientific staff will include Group Leader positions that provide a new career track to young scientists who want to focus on research rather than on the academic pressures of teaching or writing grants.

Finally, some investigator slots will be set aside for assistant professors, who often struggle to compete with more senior scientists for grants. **ISM**

Iron

continued from page 1

conducted an experiment that used three groups of mice: an experimental group that got nanoparticles loaded with chemo, a control group that got nanoparticles without chemo and a control group that got neither. The researchers made the unexpected observation that the growth of the tumors in control animals that got nanoparticles only was suppressed compared with the other controls.

Getting macrophages back on track

The researchers conducted a series of follow-up tests to characterize what was happening. Experimenting with cells in a dish, they showed that immune cells called tumor-associated macrophages were required for the nanoparticles' anti-cancer activity; in cell cultures without macrophages, the iron nanoparticles had no effect against cancer cells.

Before this study was done, it was already known that in healthy people, tumor-associated macrophages detect and eat individual tumor cells. However, large tumors can hijack the tumor-associated macrophages, causing them to stop attacking and instead begin secreting factors that promote the cancer's growth.

The study showed that the iron nanoparticles switch the macrophages back to their cancer-attacking state, as evidenced by tracking the products of the macrophages' metabolism and examining their patterns of gene expression.

Furthermore, in a mouse model of breast cancer, the researchers demonstrated that the ferumoxytol inhibited tumor growth when given in doses, adjusted for body weight, similar to those approved by the FDA for anemia treatment. Prior studies had shown that the nanoparticles are metabolized over a period of about six weeks, and the new study showed that the anti-cancer effect of a single dose of nanoparticles declined over about three weeks.

The scientists also tested whether the nanoparticles could stop cancer from spreading. In a mouse model of small-cell lung cancer, the nanoparticles reduced tumor formation in the liver, a common site of metastasis in both mice and humans. In a separate model of liver metastasis, pretreatment with nanoparticles before tumor cells were introduced greatly reduced the volume of liver tumors.

Heike Daldrup-Link

Potential clinical applications

The study's results suggest several possible applications to test in human trials, Daldrup-Link said. For instance, after surgery to remove a potentially metastatic tumor, patients often need chemotherapy but must wait until they recover from the operation to tolerate the severe side effects of conventional chemo. The iron nanoparticles lack the toxic side effects of chemotherapy, suggesting they might be given to patients during the surgical recovery period.

"We think this could bridge the time when the patient is quite sick after surgery, and help keep the cancer from spreading until they are able to receive chemotherapy," said Daldrup-Link.

The nanoparticles may also help cancer patients whose tumors can't be completely removed. "If there are some tumor cells left after surgery, the situation that cancer surgeons call positive margins, we think it might work to inject iron nanoparticles there, and the smaller tumor seeds could potentially be taken care of by our immune system," Daldrup-Link said.

The fact that the nanoparticles are already FDA-approved speeds the ability to test these applications in humans, she added.

The new findings will also help cancer researchers conduct more accurate evaluations of nanoparticle-drug combinations, Daldrup-Link said. "In many studies, researchers just consider nanoparticles as drug vehicles," she said. "But they may have hidden intrinsic effects that we won't appreciate unless we look at the nanoparticles themselves."

The study's lead author is Saeid Zanganeh, PhD, postdoctoral scholar in radiology. Other Stanford co-authors are Gregor Hutter, MD, PhD, visiting instructor in neurosurgery; Ryan Spitler, PhD, senior research scientist in radiology; Olga Lenkov, life science research assistant in the Molecular Imaging Program at Stanford; Morteza Mahmoudi, PhD, a visiting scientist in cardiology; Jukka Sakari Pajarinen, MD, PhD, postdoctoral scholar in orthopaedic surgery; Hossein Nejadnik, MD, PhD, clinical science research associate in pediatric radiology; Stuart Goodman, MD, PhD, professor of surgery; and Michael Moseley, PhD, professor of radiology.

Scientists at the Oregon Health and Science University also co-authored to the study.

The research was funded by the National Cancer Institute. Stanford's Department of Radiology also supported the work. **ISM**

Stanford Medicine

continued from page 1

other milestones, Minor said, was the opening of the Laboratory for Cell and Gene Medicine, which manufactures cell and gene therapies for use in humans. "When you have a will, when you have a vision, when you're blessed with having resources, we're able to bring together enormous talent, and to enable those very talented people to accomplish truly unique things," he said. "Already there are four first-in-humans clinical trials approved or in the final stages of being approved."

Minor also highlighted the Chan Zuckerberg Biohub, a recently announced research collaboration among scientists at Stanford, UC-San Francisco and UC-Berkeley. "The goal of the Biohub is to develop the innovative technologies, the innovative scientific approaches that are going to propel biological medical research forward in the coming decades," he said. The Biohub is funded by the Chan Zuckerberg Initiative, which aims to cure, prevent or manage all diseases by the end of the century.

These are the types of big problems Stanford Medicine scientists love to dig into, Minor said. "What really motivates us here is when someone tells us that something can't be done. We are attracted to the problems that to others appear intractable."

Seizing opportunities

Minor emphasized that although the School of Medicine has become more diverse over time — this year, about 25 percent of the incoming MD and PhD students are members of underrepresented minority groups — he sees an opportunity to deepen its commitment to diversity and inclusivity. "It's not just the pipeline. It has to also be nurturing and providing the opportunities for those students as they finish their training to enter into faculty jobs and then to succeed once they're in the faculty jobs," he said. "And that's something I know we can do here."

NORBERT VON DER GROEBEN

David Entwistle, Lloyd Minor and Christopher Dawes take part in a panel discussion during the Sept. 22 State of Stanford Medicine event.

The panelists discussed how they are responding to trends in health care. One notable tendency: patients' use of internet-enabled devices to research and monitor their health. "We're very happy that consumers have access to data," said Dawes, "but that also means we have a very informed patient population, and that creates both opportunities and challenges." Among them, said Entwistle, is making sure "we have solutions that allow people to navigate with us easily."

As Stanford Medicine expands, its leaders are also grappling with how to attract and retain top-notch staff in the Bay Area. For example, the extension of Lucile Packard Children's Hospital Stanford, scheduled to open in fall 2017, will require hiring 400 to 500 new people. "The cost of living is going to be one of our biggest challenges," Dawes said.

Advancing precision health

In the year and the decade to come, the panelists expect to continue advancing precision health. "Precision medicine, which we do here every day, is about taking genomics, big-data science, personalization of care, and bringing those to the benefit of each individual patient with a severe acute disease," said Minor. "We have no intention of backing away from that. What we see the opportunity to do is to take genomics, big-data science and personalization and apply those in a predictive and proactive way. Ten years from now, the need for personalized medicine will be much less, because we will have diagnosed diseases earlier, and therefore been able to treat them more effectively. We will even have been able to prevent diseases."

Crucial to realizing the precision health vision, the panelists said, was continuing to build strength in primary care. "Not too long ago, we had seven faculty in primary care, and now we have about 80," said Dawes. "It really comes back to what we are here for, and that is to help people — not only to get them well but to help them not to get get sick in the first place."

"We want Stanford to be known as the academic medical center where we translate fundamental research to the care our patients are receiving," said Minor. "This is the place where it happens." **ISM**

OBITUARY

Graduate student Maria Birukova dies in climbing accident

By Krista Conger

Maria Birukova, a fourth-year graduate student in the MD-PhD program at the School of Medicine, died in a climbing accident near Bear Creek Spire in the eastern Sierra Nevada Mountains. She was 26.

The accident occurred on Sept. 18 and was witnessed by her climbing partner, Ian Isaacson. Her body was recovered on Sept. 20 by members of the Inyo County Sheriff's Office, Inyo Search and Rescue and the California Highway Patrol.

Maria Birukova

Birukova, an avid mountaineer and climber, earned a bachelor's degree in biomedical engineering at Yale University. She came to Stanford in 2013 and was working in the laboratory of immunologist Paul Bollyky, MD, PhD. Earlier this year, she was awarded a Bio-X Bowes graduate student fellowship in honor of her groundbreaking interdisciplinary research.

"Maria was one of our superstars," said professor of medicine PJ Utz, MD, who directs Stanford's Medical Scientist Training Program, in which students work toward both a medical degree and a doctoral degree. "She had a background in engineering and an interest in chemistry, and we were very excited to welcome her into our program. But it was clear from the moment I met her that climbing was a major part of her life. In fact, she struggled to choose whether to attend Stanford or the University of Utah for her graduate training because in Utah the mountains are so close. We in the program are devastated that she won't now be able to fulfill her other dream of becoming a physician-scientist."

Research on biofilms

Birukova's research in the Bollyky lab focused on the role played by a virus called a bacteriophage in the formation of biofilms — viscous communities of bacteria, resistant to antibiotics and immune responses, that can colonize chronic wounds or coat medical equipment. She collaborated with researchers in the laboratory of assistant professor of chemistry Yan Xia, PhD, to design polymers and antibodies to disrupt biofilms with the aim of treating patients with deadly infections.

"The medical school community has suffered a tremendous loss," said Lloyd Minor, MD, dean of the School of Medicine. "Maria's interdisciplinary approach to the treatment of antibiotic-resistant biofilms brought to bear insights from both chemistry and immunology in an attempt to devise new treatments for patients with few other options. Her work was a wonderful example of Stanford's focus on translational medicine, and she will be greatly missed, both professionally and personally."

In addition to finding time to climb, Birukova was a consulting project manager for the Stanford Healthcare Consulting Group, a nonprofit, volunteer-run organization devoted to improving patient care through quality- and performance-improvement projects. Birukova was also a 2015-16 Graduate Voice and Influence Program Fellow through Stanford's Clayman Institute for Gender Research. She was a native Russian speaker and, while at Yale, spent time transcribing taped oral interviews with Russian oil workers into written Russian documents.

"Maria was a very dynamic, interested and interesting person who really engaged with the Stanford community in a number of ways," said Bollyky, an assistant professor of medicine and of microbiology and immunology. "In addition, she was an outstanding scientist. Her research focused on the intersection between microbiology, structural biology and physical chemistry in biofilms. It was very novel, and she was incredibly energetic and passionate about developing new therapies for patients with chronic wounds. Her loss leaves a hole in her graduate class, as well as in my lab."

Birukova was born on May 31, 1990, in Moscow, Russia. She attended the University of Chicago Laboratory Schools in Chicago. She is survived by her parents, Konstantin Birukov, MD, PhD, and Anna Birukova, MD, who are both on the faculty of the Pritzker School of Medicine at the University of Chicago. ISM

Manu Prakash wins prestigious grant from MacArthur Foundation

By Amy Adams

Manu Prakash, PhD, an assistant professor of bioengineering at Stanford, has been named one of the 2016 fellows of the John D. and Catherine T. MacArthur Foundation.

The fellowships, popularly known as "genius grants," are awarded to scholars who show exceptional creativity in their work and the prospect for still more in the future. It includes a $625,000 stipend over five years, designed to provide recipients with the flexibility to pursue their activities in the absence of specific obligations.

The MacArthur Foundation recognized Prakash for his research that is "driven by curiosity about the diversity of life forms on our planet and how they work, empathy for problems in resource-poor settings, and a deep interest in democratizing the experience and joy of science globally."

"Manu Prakash is not only one of the most innovative scientists of our day, he is also using his interdisciplinary expertise to improve human health around the world," said Stanford President Marc Tessier-Lavigne, PhD. "He harnesses a wide array of technologies, including optical physics, computer science, fluid dynamics, biology and chemistry, to solve tangible human and scientific problems. It is fitting that his creative approach to applying scientific principles has been recognized as true genius by the MacArthur Foundation."

Prakash almost didn't pick up the phone when the MacArthur Foundation called. He was caring for his 4-month-old twins at the time. "I was very sleep-deprived when the phone rang," he said. "My main reaction is that it is a very humbling experience because there are so many people in the world doing amazing work."

Driven by curiosity

Prakash said his research has been driven by curiosity about the world rather than answering a particular question. "I've done science the way I've wanted to do science," he said. "Sometimes it's hard to convince others that we are taking the right approach. This award gives me the flexibility to not think about those bounds."

Prakash's studies problems in organismal biology through the lens of physics. He also builds tools and approaches to do field science that are both low-cost and extremely powerful, bringing science out of the lab and to parts of the world where traditional tools aren't feasible.

One example of this approach is a microscope made out of paper with a glass bead for a lens, called the Foldscope. It costs less than a dollar to make and has now been distributed by his lab to more than 50,000 people in 135 countries who use the tool in research and education.

L.A. CICERO

Manu Prakash, a bioengineer, will receive $625,000 over five years from the MacArthur Foundation.

"What the community has done with the Foldscope is phenomenal," said Prakash, who requests that people who receive Foldscopes share back on what they've learned with the Foldscope community.

People around the world have used Foldscopes for projects exploring diseases in bees, documenting pollen grains in urban landscapes, mapping biodiversity of microscopic organisms, detecting cervical cancer, and teaching hygiene and sanitation and in hands-on education, among many other projects.

"Manu's work could help solve some of the biggest issues facing us in global health," said Lloyd Minor, MD, dean of the School of Medicine. "His creativity has led to powerful, low-cost technologies that people in remote locations can use to study and treat disease in their communities. These are the kinds of solutions that will bring real change to health-care challenges."

An eye toward global health

Prakash said that many of his ideas come from his travels and from his childhood growing up in India. "Being in the field gives meaning to working in global health," Prakash said. "It teaches you empathy, a driving force so strong that it transforms ideas into actions."

An example of this is his work designing tools to track and detect mosquito species by people around the world. This work would allow communities to survey mosquitoes at large scale and track the vectors for some of the most deadly diseases. In a few months, the Prakash lab will start testing some of these tools in a field site in Madagascar.

"Manu's contributions to global health are an inspiration to us all," said Persis Drell, PhD, dean of the School of Engineering. "It is through precisely the kinds of creative innovations in technology that Manu is developing that we can have significant impact on the world's urgent challenges."

Some of his other work is more whimsical in origin. When Prakash's wife gave him a mechanical music box as a gift, he realized that the inner workings of the toy — with its tiny wheel spinning pins of various sizes — could be used to drive a miniature chemistry kit akin to how old mechanical computers used to work. That kit won him the Science Play and Research Kit (SPARK) competition, jointly sponsored by the Gordon and Betty Moore Foundation and the Society for Science & the Public. The award was for the device's possibility as a child's toy, but it could also run chemical assays in remote locations, such as testing water purity or running diagnostics tests.

"Often a challenge in technology deployment is building engaged local communities that take ownership of ideas and deployment. I'd started thinking about this connection between science education and global health," Prakash said. "The things that you make for kids to explore and experience science are also exactly the kind of things that you need in the field because they need to be robust, scalable and they need to be highly versatile."

Another series of projects that began with his PhD work pioneering microfluidic bubble logic involves the dynamics of water droplets, whose mysterious movement had captivated Prakash. He figured out how the surface dynamics of droplets result in their dancelike interactions.

He then went on to apply what he'd learned about manipulating water droplets to develop a computer powered by the motion of droplets. "Our goal is not to compete with electronic computers or to operate word processors on this," Prakash said. "Our goal is to build a completely new class of computers that can precisely control and manipulate physical matter at mesoscale."

Prakash said that he doesn't know exactly what research he will pursue with his award. "I can't say what this will mean to my science as yet, but I know for sure we have a lot of ideas brewing," he said.

Prakash is also a member of the interdisciplinary institutes Stanford Bio-X, Stanford ChEM-H and the Stanford Woods Institute for the Environment. Stanford's Department of Bioengineering is jointly operated by the School of Medicine and the School of Engineering. ISM

Physician, author Abraham Verghese awarded humanities medal

By Tracie White

Abraham Verghese, MD, professor of medicine at the Stanford School of Medicine, received a National Humanities Medal at a White House ceremony Sept. 22.

"Abraham Verghese is not only an exemplary clinician, he is an exemplary humanist," said Stanford President Marc Tessier-Lavigne. "Every day in the classroom, he teaches his students that professions such as medicine benefit from an understanding of the human condition. We are so proud that his breadth of scholarship has been recognized with this honor."

Inaugurated in 1997, the National Humanities Medal "honors individuals or groups whose work has deepened the nation's understanding of the human experience, broadened citizens' engagement with history, literature, languages, philosophy, and other humanities subjects," according to the National Endowment for the Humanities website. As many as 12 medals are awarded each year.

The organization said Verghese is receiving the medal "for reminding us that the patient is the center of the medical enterprise. His range of proficiency embodies the diversity of the humanities; from his efforts to emphasize empathy in medicine, to his imaginative renderings of the human drama."

"I am humbled and excited by this honor," said Verghese, who is the Linda R. Meier and Joan F. Lane Provostial Professor. "The names of previous recipients include writers I most admire. It's a wonderful affirmation of a path that in the early years I wasn't sure was the right path, even though it was one I felt compelled to follow."

The human touch

Verghese is a critically acclaimed, best-selling author and a physician with an international reputation for his emphasis on empathy for patients in an era in which technology often overwhelms the human side of medicine.

"This is a special honor for a physician," said Lloyd Minor, MD, dean of the School of Medicine. "Through his writings and his work as a physician, Abraham has worked to battle what he has seen as a lack of humanism in modern medicine. The courage to follow his own path, and the compassion he has brought to his work, have made the world a better place."

In his first book, *My Own Country: A Doctor's Story*, Verghese focused on his early years as an orderly, his caring for terminal AIDS patients and the insights he gained from the relationships he formed and the suffering he witnessed.

"I felt strongly then and now that what I was writing about, and my interest in the human experience of being ill or caring for the ill, was as much a part of medicine as knowledge of the function of the pancreas, for example," said Verghese, who is also a vice chair of Stanford's Department of Medicine. In addition, Verghese directs the Stanford interdisciplinary center, Presence, which reflects these interests.

The National Endowment for the Humanities manages the nomination process for the National Humanities Medal on behalf of the White House. Each year, the NEH invites nominations from individuals and organizations across the country. The National Council on the Humanities, NEH's presidentially-appointed and Senate-confirmed advisory body, reviews the nominations and provides recommendations to the president, who selects the recipients.

Joining Verghese as medal recipients this year were two other writers with Stanford connections: poet Louise Glück, a visiting faculty member in the Department of English; and Elaine Pagels, a religious historian and author of the *Gnostic Gospels* and *Beyond Belief: The Secret Gospel of Thomas,* who earned both bachelor's and a master's degrees from Stanford. **ISM**

CHERISS MAY / NDEMAY MEDIA GROUP

President Barack Obama presented Abraham Verghese with a National Humanities Medal on Sept. 22.

OF NOTE

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

LEAH BACKHUS, MD, associate professor of cardiothoracic surgery, was selected to serve a three-year term as a member of the Patient-Centered Outcomes Research Institute's Advisory Panel on Improving Healthcare Systems. The panel advises the institute on research-funding decisions. Backhus is the chief of thoracic surgery at the Veterans Affairs Palo Alto Health Care System. Her research focuses on imaging following treatment for lung cancer and on cancer survivorship.

Leah Backhus

Leonore Herzenberg

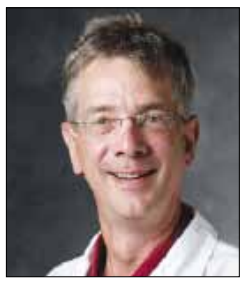
Laurence Katznelson

Paul Kwo

Richard Lafayette

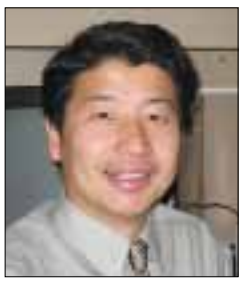
David Lee

Lei Stanley Qi



PJ Utz

Cornelia Weyand



Sean Wu

Jiangbin Ye

LEONORE HERZENBERG, D.Sc-equivalent, professor of genetics and the Department of Genetics Flow Cytometry Professor, was named an honorary fellow of the Royal Microscopical Society. She was recognized for her contributions to the development of the fluorescence-activated cell sorter, which is used to diagnose leukemia and in stem cell transplantation.

WILLIAM HIESINGER, MD, was appointed assistant professor of cardiothoracic surgery, effective Aug. 1. His clinical interests include thoracic transplantation, medical circulatory support and endovascular aortic surgery.

LAURENCE KATZNELSON, MD, professor of neurosurgery and of medicine and associate dean of graduate medical education, has received the 2017 Outstanding Educator Laureate Award from the Endocrine Society. The honor, which includes a $3,000 prize, recognizes exceptional achievement as an educator in endocrinology and metabolism. Katznelson is also the medical director of the Stanford Pituitary Center.

PAUL KWO, MD, was appointed professor of medicine, effective Aug. 1. His research focuses on therapy for hepatitis B and C and on liver transplant outcomes.

RICHARD LAFAYETTE, MD, was promoted to professor of medicine, effective July 1. He directs the Stanford Glomerular Disease Center. He investigates new therapies for renal disease and performs collaborative studies of the immunological basis of glomerular injury.

DAVID LEE, MD, associate professor of medicine, was elected president of the Western States Affiliate of the American Heart Association. As president, he plans to advocate for healthy habits, particularly in children; enhanced regulation of tobacco and e-cigarette sales; expanded access to CPR training; and mandating healthy foods in schools.

SARAH MADISON, MD, was appointed assistant professor of anesthesiology, perioperative and pain medicine, effective Feb. 1. Her research focuses on regional anesthesia and on treating acute pain during surgery.

LEI STANLEY QI, PhD, assistant professor of bioengineering and of chemical and systems biology, was named to the 2016 class of Pew biomedical scholars, a program that supports exceptional early-career scientists. He will receive $60,000 a year for four years. His research focuses on CRISPR development for transcription and epigenetic regulation and on genomic reprogramming of immune cells to identify and kill cancer cells.

HOLLY TABOR, PhD, was appointed associate professor of medicine, effective June 1. She is the associate director for clinical ethics and education at the Stanford Center for Biomedical Ethics. Her research focuses on ethical issues related to genetics and genomics.

PJ UTZ, MD, professor of medicine, has joined the scientific advisory board of the Arthritis National Research Foundation, which provides grants for research on arthritis and other autoimmune disorders. He directs Stanford's Medical Scientist Training Program and is the founder and director of the Stanford Institutes of Medicine Summer Research Program for high school students. His research focuses on improving the understanding and treatment of autoimmune disorders.

CORNELIA WEYAND, MD, professor of medicine and chief of immunology and rheumatology, was named a Notable Woman in Science and Medicine by the Max Delbrück Center for Molecular Medicine in the Helmholtz Association in Berlin, Germany. She delivered a lecture in July on protective and pathogenic immune responses and provided mentoring sessions for students, fellows and junior faculty.

SEAN WU, MD, PhD, was promoted to associate professor of medicine, effective April 1. He treats patients with cardiac diseases, and his research uses stem cells to try to develop treatments for heart failure and cardiac-rhythm disorders.

JIANGBIN YE, PhD, was appointed assistant professor of radiation oncology, effective Aug. 1. His research focuses on tumor cell metabolism, with the goal of targeting metabolic pathways to improve cancer treatments. **ISM**