INSIDE STANFORD MEDICINE

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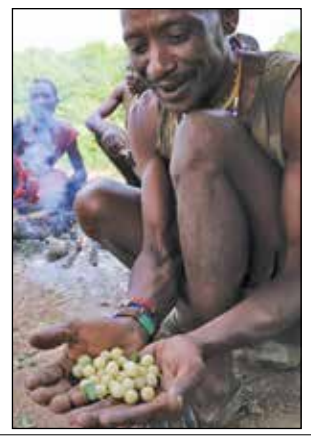


The gut-microbe diversity of a population of hunter-gatherers in Tanzania varies seasonally, a study found.

Page 5

For Stanley Falkow, a legacy of mentorship

By Kathy Zonana

When Stanley Falkow was awarded a National Medal of Science last year at the White House, he was lauded not only for "his monumental contributions toward understanding how microbes cause disease and resist the effects of antibiotics," but also for a lesser-known, albeit perhaps equally significant, legacy: "his inspiring mentorship that created the field of molecular microbial pathogenesis."

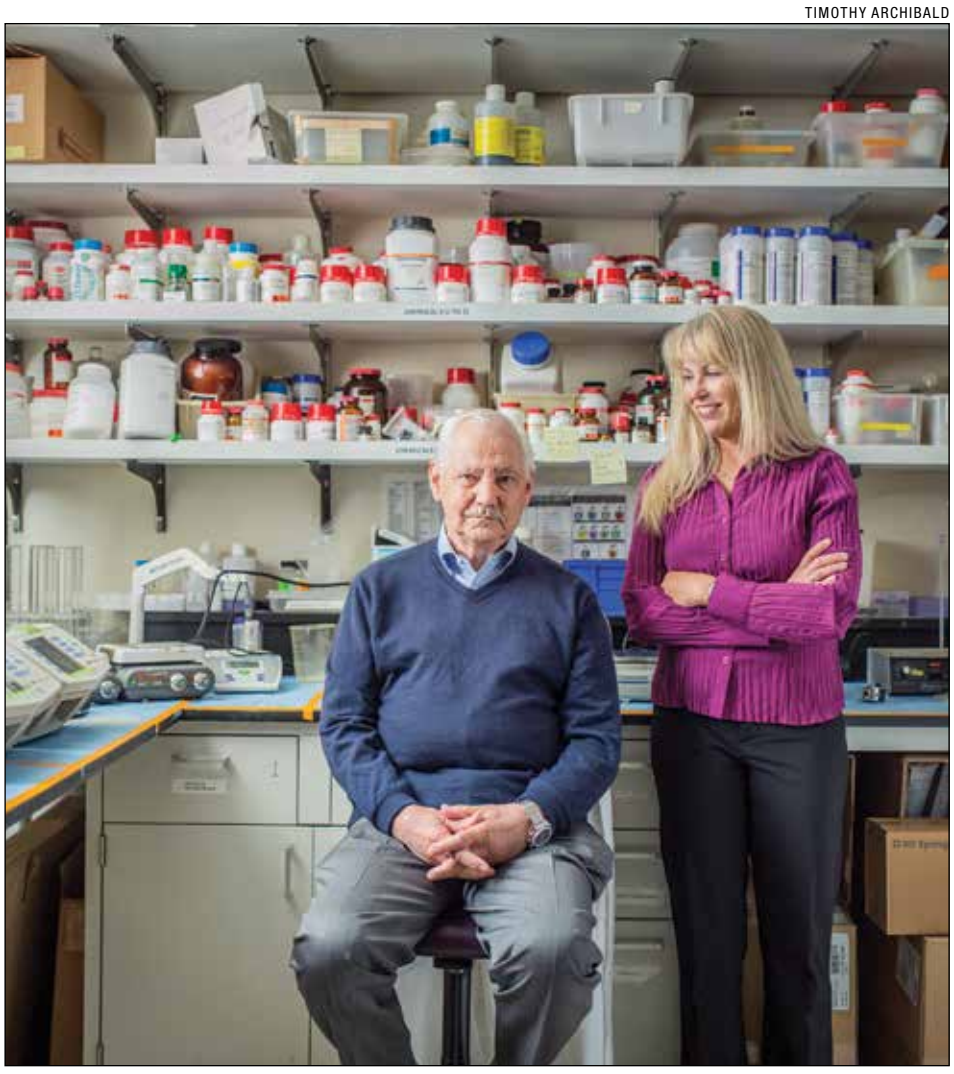
Over the course of his career, Falkow, PhD, a professor emeritus of microbiology and immunology at the School of Medicine, became known for his generosity and inspiration as an adviser to young researchers trying to forge careers in science.

He has mentored more than 100 graduate students and postdoctoral scholars in his lab. Three of them — Manuel Amieva, MD, PhD, associate professor of pediatrics and of microbiology and immunology; Denise Monack, PhD, professor of microbiology and immunology; and David Relman, MD, professor of medicine and of microbiology and immunology — have made their faculty careers at Stanford.

Although Falkow is quick to deflect any credit, these faculty members are deepening his legacy at Stanford in several ways: in the teaching of microbiology, in research that underscores the impact of microbes on human health, and in big, connect-the-dots ideas that bridge basic science and medicine.

The Robert W. and Vivian K. Cahill Professor in Cancer Research, Emeritus, Falkow "is one of the most generous people with his ideas and with his time and with his energy and of course with all of his other resources as well," Relman said. "He never has done any of that giving with anything other than obvious evidence of joy. And it's not just the joy of being a generous person, but the joy of sharing interesting ideas and having such a wonderful job, so that you can't help but leave his room feeling like we are so lucky to get to think about these interesting questions and work with such great people and try to do useful things."

TIMOTHY ARCHIBALD



Stanley Falkow hired Denise Monack as a lab technician in 1984. Now, she's a professor at Stanford.

But first, how *not* to mentor

Falkow's journey to becoming a master mentor began with a mistake. He was in his first faculty job, at Georgetown University, and a former co-worker from Walter Reed Army Institute of Research had, at the urging of Falkow and others, just earned a PhD in a colleague's lab.

"The day he got his degree, he walked into my office and said, 'Falkow, I hope you're satisfied, because this is for you and not for me,'" Falkow remembered. "I was stunned. And he said, 'All I wanted to do was go into the lab every day, do experiments and go home, and now my life is ruined because I can't go home and enjoy it.'"

Falkow would never again be so directive, or push someone toward an aspiration that might not be theirs. "I decided the best thing to do was to just listen," he said. "And in the years when I listened, I listened very carefully to what my students said, and then I told them to do what they said they wanted to do. And they usually thought I was very wise."

Amieva recalled visiting Falkow's office as a postdoctoral scholar to talk about his research. "He would just listen and then he would make some insight that could have several meanings," Amieva said. "It was almost like some parable. I would leave trying to figure out what he meant and spend the whole day doing it. It's a technique he uses to make you think through things."

On the side of microbes

Amieva was first inspired by Falkow during medical school. "I was a little bit disappointed with the classes in medical school; they were very dry and about all these facts, and I remember being a little bit angry about the lack of inspiration," he said. "And then I took a class from Stanley Falkow.

See FALKOW, page 6

Technique enhances privacy for genetic-study participants without compromising science

By Krista Conger

It is now possible to scour complete human genomes for the presence of disease-associated genes without revealing any genetic information not directly associated with the inquiry, Stanford researchers say.

This "genome cloaking" technique, devised by biologists, computer scientists and cryptographers at the university, ameliorates many concerns about genomic privacy and potential discrimination based on an individual's genome sequence.

See PRIVACY, page 7

SCIENCE PHOTO / SHUTTERSTOCK.COM

Popular mouse model of human immune system unsuitable for stem cell studies, researchers find

By Krista Conger

A type of mouse widely used to assess how the human immune system responds to transplanted stem cells does not reflect what is likely to occur in patients, according to a study by researchers at the School of Medicine.

The researchers urge further optimization of this animal model before making decisions about whether and when to begin wide-scale stem cell transplants in humans.

Known as "humanized" mice, the animals have been engineered to have a human, rather than a murine, immune system. Researchers have relied upon the animals for decades to study, among other things, the immune response to the transplantation of pancreatic islet cells for diabetes and skin grafts for burn victims.

However, the Stanford researchers found that, unlike what would occur in a human patient, the humanized mice are unable to robustly reject the transplantation of genetically mismatched human stem cells. As a result, they can't be used to study the immunosuppressive drugs that patients will likely require after transplant. The researchers conclude that the humanized mouse model is not suitable for studying the human immune response to transplanted stem cells or cells derived from them.

"In an ideal situation, these humanized mice would reject foreign stem cells just as a human patient would," said Joseph Wu, MD, PhD, director of Stanford's Cardiovascular Institute and professor of cardiovascular medicine and of radiology. "We could then test a variety of immunosuppressive drugs to learn which might work best in patients, or to screen for new drugs that could inhibit this rejection. We can't do that with these animals."

See MOUSE, page 7

STEVE FISCH

Joseph Wu and his collaborators found that a widely used mouse model doesn't reflect what is likely to occur in humans who receive stem cell transplants.

Statewide, race of infants influences quality of their hospital care

By Erin Digitale

Infants' racial and ethnic identities influence the quality of medical care they receive in California's neonatal intensive care units, a study from the School of Medicine has found.

The study, which examined medical care of more than 18,000 of the state's smallest babies at 134 California hospitals, was published Aug. 28 in *Pediatrics*.

The disparities were not uniform: At some California hospitals, infants from vulnerable populations received worse care than white infants, while at others, they received better care than whites. In general, however, the hospitals with the best outcomes for their patients also delivered better care to white infants. In addition, the study found that black and Hispanic infants were more likely than white infants to receive care in poor-quality NICUs.

MAESSE PHOTOGRAPHY / SHUTTERSTOCK.COM

Disparities exist in how babies of different racial and ethnic origins are treated in California's neonatal intensive care units, according to a new study.

"There's a long history of disparity in health care delivery, and our study shows that the NICU is really no different," said the study's senior author, Jochen Profit, MD, associate professor of pediatrics. "Unconscious social biases that we all have can make their way into the NICU. We would like to encourage NICU caregivers to think about how these disparities play out in their own units and how they can be reduced."

The smallest babies

The study used data from the California Perinatal Quality Care Collaborative, which has collected information on 95 percent of premature births in the state. The study included 18,616 babies whose birth weights were less than 3.3 pounds, a category known as very low birth weight, and who were born between the beginning of 2010 and the end 2014. The research excluded infants born extremely premature (before 24 weeks of pregnancy), those who died before 12 hours of age and those with severe congenital abnormalities.

Profit and his colleagues used an index they had previously developed and validated to measure NICU care. To use the index, called Baby-MONITOR, each infant's medical records are evaluated and scored on nine yes-or-no questions, all of which have been shown in prior research to reflect the quality of medical care. Some questions assess whether patients received aspects of NICU care that are in keeping with standard medical practices for premature babies, such as being examined for an eye disease called retinopathy of prematurity, or receiving steroids before birth to help mature their lungs. Other questions assess specific medical outcomes, such as experiencing a hospital-acquired infection or growing at a healthy rate. All questions are worded such that better outcomes produce higher scores.

The analysis then adjusts scores to account for the length of the mother's pregnancy, whether the mother received prenatal care, whether the baby was from a single or multiple birth, the baby's 5-minute Apgar score (a quick assessment of the infant's physical health at birth) and whether delivery was by cesarean section.

Scores were also statistically adjusted to reflect the fact that some hospitals cared for sicker babies, on average, than others. The final score for each hospital, and for each group of patients within a hospital, reflects whether the hospital did the same, better or worse than would be expected in addressing their patients' medical problems. Scores were calculated separately for white, black, Hispanic, Asian and "other" infants and referenced for each subgroup against whites.

When researchers analyzed the population of very low birth weight infants in their study, Hispanic infants and those with "other" ethnicity had lower Baby-MONITOR scores than white infants, while black and Asian infants did not have significantly different scores than whites. However, across the state, white infants scored higher on measures of whether standard medical practices were being followed. For instance, 89 percent of white infants and 88 percent or Asian infants in the study received steroids before birth to mature their lungs, while 87 percent of Hispanic infants and 85 percent of black infants got the same treatment. The difference remained statistically significant after adjusting for possible confounding factors.

Jochen Profit

Black infants had lower rates than white infants of receiving any human milk at discharge — an indicator of worse outcomes — but also had better outcomes in some areas, including faster growth rates and lower rates of chronic lung disease and collapsed lung. Hispanic infants did worse than whites on all components of the score except collapsed-lung rates.

Across NICUs, those that provided the poorest quality of care tended to have the smallest disparities between ethnicities; in some, blacks fared better than white infants. As quality scores rose across hospitals, white infants tended to do better.

The researchers also found that although racial and ethnic differences in NICU care were fairly small when examined across California as a whole, some individual hospitals had large gaps in how they cared for infants from different racial and ethnic backgrounds.

Individualizing care

Addressing the disparities will require a nuanced approach, Profit said. "It's really important for NICUs to individualize care to the patient population they see," he said.

> "There's a long history of disparity in health care delivery."

For instance, Hispanic families who are primarily Spanish-speaking may be experiencing language barriers that make it harder for parents to ask questions and act as advocates for their infants. "For them, having access to translation and personnel who speak Spanish is really critical," he said. Hospitals serving a larger proportion of African-American infants may have different issues they need to address.

The next step, Profit said, is to help California's NICUs identify ways in which they can each make progress in treating all infants more equitably. "Our goal is to develop a dashboard of disparity measures for NICUs throughout California so that each can see how they're performing for infants of different races and ethnicities in comparison to their peers," he said. The feedback will become part of the work of the California Perinatal Quality Care Collaborative, which has organized successful quality-improvement initiatives to help NICUs across the state improve the medical care they deliver. The researchers are also working with the Vermont Oxford Network, a sister organization that monitors NICUs across the country to provide similar feedback to hospitals nationwide.

"We need to continue to identify vulnerable populations, make sure they get their needs met and find better ways to engage all families in our care," Profit said.

Hospital care during the newborn period is not the largest contributor to health disparities that minority infants experience, Profit noted, estimating that socioeconomic and biological differences likely make a larger contribution. Nevertheless, that does not mean disparities in medical care should be ignored, he added.

"For many of these infants, their time in the NICU sets them on track for their entire life," Profit said. "If we can get things right early on, that could have a huge long-term effect."

Other Stanford collaborators on the research are Jeffrey Gould, MD, professor of pediatrics; biostatistician Mihoko Bennett, PhD; Ciaran Phibbs, PhD, associate professor of pediatrics; and Henry Lee, MD, associate professor of pediatrics. Profit, Gould and Lee are members of Stanford's Child Health Research Institute.

Researchers at Duke University School of Medicine and the University of California-Santa Cruz also contributed to the work.

The study was supported by grants from the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

Stanford's Department of Pediatrics also supported the work. **ISM**

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STANFORD MEDICINE

Cardiovascular symposium will bring together experts from Stanford, China

By Tracie White

The Stanford-China Cardiovascular Research Symposium will take place Sept. 21-22 at the medical school's Li Ka Shing Center for Learning and Knowledge.

The two-day conference, which is free and open to the public, will bring together a variety of experts in cardiovascular medicine from the United States and China to share knowledge that can advance heart health. The conference aims to foster communication between students, postdoctoral scholars, clinicians and researchers to share expertise in order to facilitate future collaborations between China's leading cardiovascular treatment and research institutions and Stanford, said Joseph Wu, MD, PhD, director of the Stanford Cardiovascular Institute, which is organizing the event.

"This conference draws cardiovascular experts from many of China's most esteemed hospitals and universities, providing a valuable opportunity to share knowledge with Stanford and U.S. experts that will improve international collaboration on cardiovascular research and clinical care," Wu said.

One of the keynote speakers is Victor Dzau, MD, president of the National Academy of Medicine and a professor of medicine at the Duke University School of Medicine.

Topics to be discussed include: Advances in cardiac surgery, vascular surgery, pe-

See SYMPOSIUM, page 3

Study on what leads to chronic migraines seeks participants

By Bruce Goldman

Researchers at the School of Medicine are recruiting participants for a clinical trial aimed at finding out why some people who suffer occasional migraine headaches progress to a chronic stage of frequently occurring migraines.

The trial, underway for about two years now, has recruited more than 200 participants, and investigators are seeking another 300. Candidates must be 18 years or older. The researchers want to enroll not just people who experience migraines or other headache types, but also people who don't have headaches at all to serve as control subjects.

ALLIANCE / SHUTTERSTOCK.COM

Of the 37 million Americans who suffer from migraines, a few million progress to a chronic stage of having them more often than not. Investigators hope to find out why.

"Our understanding of headaches lags well behind that for many other neurological conditions, which is sad since it's the most common neurologic complaint a doctor will see," said the trial's principal investigator, Robert Cowan, MD, professor of neurology and neurological sciences.

"Everyone knows at least someone who suffers with migraine," said Cowan, who holds the Betty Higgins Family Foundation Professorship in Headache Medicine and is the director of Stanford's Headache and Facial Pain Center.

Of the 60 million people in the United States who get headaches, he said, 37 million of them get migraines — intense throbbing headaches often accompanied by nausea and/or hypersensitivity to sound and light. Among a substantial fraction of migraine sufferers, this painful experience is preceded by a characteristic premonitory, often visual, disturbance known as an aura.

Robert Cowan

Costly condition

Cowan experienced his first migraine at age 5. More typically, though, migraines hit people hardest during their most productive years. There's an uptick of migraine incidence in the teen years and early adulthood, when people are getting their educations, starting families and building careers.

For as-yet unknown reasons, women are three times as likely as men to suffer from migraines.

The bulk of the estimated $15 billion to $30 billion annual cost of headaches to the U.S. economy is accounted for by loss of work productivity, said Cowan. These people, who experience symptoms more days than not, number in the millions.

For the majority of patients with migraines, the most effective prescriptions are lifestyle recommendations, he said. "Don't skip meals, keep regular hours and get daily exercise — don't just sit around."

Better understanding sought

Why some people are susceptible to migraines and why some — but not others — who do get them become more susceptible over time isn't well understood, Cowan said.

"The basic question we're addressing is: Why do some people get occasional headaches while others get headaches with increasing severity and disability? Are chronic migraines just episodic migraines that occur more often? We suspect not," he said.

The investigators will conduct rigorous analyses of trial participants' blood, brain function and cerebral spinal fluid in an effort to find factors that correlate with migraine susceptibility, severity and frequency.

Participants will be asked to fill out medical questionnaires and report to the Stanford campus for a minimum of two or three roughly one- to two-hour medical visits. (Free parking will be provided.) The investigators will draw participants' blood and record their brain activity using functional magnetic resonance imaging and perform lumbar punctures, also known as spinal taps. Participants who agree to undergo fMRI or lumbar punctures will receive compensation of $50 apiece for each procedure.

"If we can find risk factors that predispose some migraine patients' progression from an episodic to a chronic condition, and use these to identify at-risk patients, it may provide insight into personalized treatments to prevent episodic headaches from becoming chronic," said Cowan.

Prospective participants who want to learn more about the trial or about their potential eligibility for it are encouraged to contact trial coordinator Bharati Sanjanwala at bharatis@stanford.edu.

The trial is funded by the Sun Star Foundation. **ISM**

Latest Intermountain, Stanford seed grant recipients announced

The recipients of five new seed grants have been announced by Stanford Medicine and Intermountain Healthcare.

In 2016, the two organizations began collaborating on joint clinical, research and education projects. Intermountain Healthcare is a not-for-profit health system based in Utah.

The one-year seed grants of up to $75,000 are being awarded to projects jointly led by principal investigators from Stanford and Intermountain. The grants will take effect Sept. 1.

Following are the names of the grant recipients and their project titles:

- Alex Sox-Harris, PhD, associate professor of research at Stanford, and Stephen Warner, MD, Intermountain — Setting a foundation for collaborative surgical health services research at Stanford Health Care, Intermountain Healthcare and the Veterans Health Administration.
- Ian Brown, MD, clinical assistant professor of emergency medicine at Stanford, and Joseph Bledsoe, MD, Intermountain — Electronic decision support for the diagnosis and treatment of acute pulmonary embolism in the emergency department.
- Alan Schroeder, MD, clinical associate professor of pediatrics at Stanford, and Eric Coon, MD, Intermountain — Optimizing value in bronchiolitis: The bronchiolitis follow-up intervention trial.
- Purvesh Khatri, PhD, assistant professor of medicine and of biomedical data science at Stanford, and Patrick Carroll, MD, Intermountain — Early detection of neonatal early onset sepsis using the Sepsis MetaScore: A genomic analysis of cord blood.
- Marcy Winget, PhD, clinical associate professor of medicine at Stanford, and Brenda Reiss-Brennan, PhD, Intermountain — Pragmatic design for enhanced team-based primary care.
- Aruna Subramanian, MD, clinical associate professor of medicine at Stanford, and Brandon Webb, MD, Intermountain — Repurposing an old drug for a new epidemic: Ursodeoxycholic acid and *C. difficile* infection. **ISM**

KRIS NEWBY

Moon upstages sun

A crowd gathered outside the Clark Center on Aug. 21 to view the eclipse, which blocked out about 75 percent of the sun in the Bay Area. The cloudy skies over campus cleared just in time that morning for viewers to glimpse the extraterrestrial phenomenon. The next time a solar eclipse will come to the United States will be April 8, 2024. But California won't be in its path.

Symposium

continued from page 2

ripheral arterial disease, interventional cardiology, basic science and clinical trials.

Among the other speakers are Stanford's Joseph Woo, MD, professor of cardiothoracic surgery, who will give a talk titled "The convergence of biologic and surgical reconstructive therapies for cardiovascular diseases," and Haibo Zhang, MD, PhD, deputy director of cardiac surgery at Beijing Anzhen Hospital, Capital Medical University, who will speak on heart failure and the heart-transplant program at his hospital.

"Sharing complementary insights to advance cardiovascular health will benefit literally billions of people worldwide, not just in the two countries," Wu said.

The conference is sponsored in part by the Chi-Li Pao Foundation. **ISM**

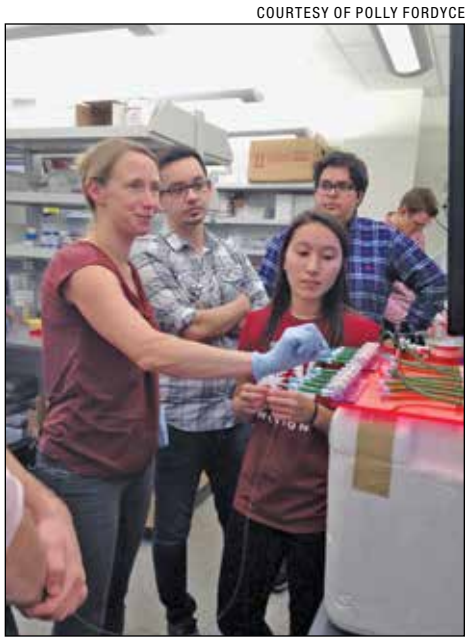
Students design small tools to tackle big scientific challenges

By Nathan Collins

Team Traptasia had a problem: The tiny baby sea anemones they were trying to ensnare are, unlike their adult forms, surprisingly powerful swimmers. They are also, as team member and chemical engineering graduate student Daniel Hunt put it, "pretty squishy little deformable things."

Previous attempts to trap the anemones, called Aiptasia, while keeping them alive long enough to study under a microscope had ended in gruesome, if teensy, failure.

COURTESY OF POLLY FORDYCE



Polly Fordyce (left) and graduate students Louai Labanieh, Sarah Lensch and Diego Oyarzun discuss the design of a microfluidic device built to study coral bleaching.

But Traptasia had to make it work. Cawa Tran, then a postdoctoral scholar, and her research into climate change's effects on coral bleaching were depending on them. (Sea anemones, it turns out, are a close relative of corals, but easier to study.)

And then there was the matter of the team's grades to consider, along with the outcome of an experiment in the "democratization" of a powerful set of tools known as microfluidics.

Democratizing science

Team Traptasia was part of a microfluidics course dreamed up by Polly Fordyce, PhD, an assistant professor of genetics and of bioengineering and a Stanford ChEM-H faculty fellow.

At the time, she was feeling a bit frustrated.

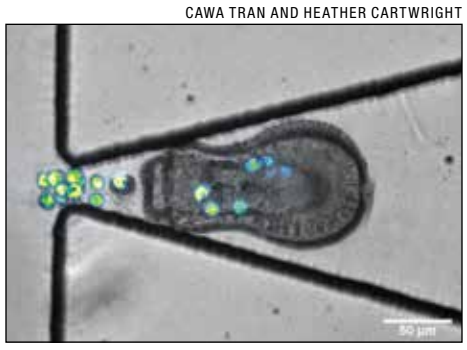
"Microfluidics has the potential to be this really awesome tool," Fordyce said. That's because microfluidic devices shrink equipment that would normally fill a chemistry or biology lab bench down to the size of a large wristwatch, saving space and materials, not to mention time and money. They also open up entirely new ways to conduct biological research — trapping baby sea anemones and watching them under a microscope, for example. But making high-quality devices takes expertise and resources most labs don't have.

"There's this big chasm between the bioengineers that develop devices and the biologists that want to use them," Fordyce said. Bioengineers know how to design sophisticated devices and biologists have important questions to answer, but there is little overlap between the two.

To bridge the gap, Fordyce invited biology labs to propose projects to students in her graduate-level microfluidics course. The idea, she said, was to give students real-world experience while giving labs access to technology they might not have the time, money or expertise to pursue otherwise.

In fact, the desire to break down disciplinary boundaries was something that attracted her to Stanford and to ChEM-H in the first place. "One of the reasons that I came to Stanford and ChEM-H was that I really love the idea of having interdisciplinary institutes that attempt to cross the boundaries between disciplines," she said.

CAWA TRAN AND HEATHER CARTWRIGHT



A young Aiptasia sea anemone ejects algae (highlighted in blue-green) in response to changing water conditions.

Ultimately, researchers from four labs took part, including Tran, who was working in the lab of John Pringle, PhD, a professor of genetics. Fordyce will be describing her experiences teaching that class in an upcoming paper, which she hopes will provide a blueprint for people eager to help others make use of microfluidics tools.

Shrinky Dinks vs. Aiptasia

Before linking up with Fordyce's class, Tran had been working with Heather Cartwright, core imaging director at the Carnegie Institution for Science's Department of Plant Biology. Together they tried a more do-it-yourself approach involving the children's toy Shrinky Dinks, an approach first proposed by Michelle Khine at the University of California-Irvine.

The effort did not work. "We got some movies. They were mostly end-of-life movies," Cartwright said.

"This year was successful beyond my dreams."

If Tran and Cartwright managed to trap Aiptasia, their Shrinky Dink device crushed or twisted the sea anemones apart. So when Fordyce approached them to work with what would become Team Traptasia — graduate students Salil Bhate, Hunt, Louai Labanieh, Sarah Lensch and Will Van Treuren — and Stanford's Microfluidics Foundry, they jumped at the chance.

A non-smashing success

Team Traptasia, Tran said, solved her problem "completely."

After several rounds of design, troubleshooting and testing, Team Traptasia built a microfluidic device that kept Aiptasia alive and healthy long enough to study. As a result, the researchers could actually watch the effects of rising water temperature and pollution on living sea anemones and their symbiotic algae — something that has never been done before. Tran, Cartwright and Team Traptasia will publish their findings soon, Tran said.

Other teams have helped labs design devices to study how the parasite that causes toxoplasmosis infects human cells, to trap and study placental cells, and to isolate single cells in tiny reaction chambers for detailed molecular biology studies.

Tran said the device Team Traptasia came up with could provide opportunities for the Pringle lab, as well as in education. Now an assistant professor at California State University- Chico, Tran said she'll be using the device with undergraduates there. "Basically, this device has given me the opportunity to train the next generation of biologists" in a new, research-focused way, she said.

Hunt, the chemical engineering student in Team Traptasia, said that his own research on intestinal biology could benefit from microfluidics. "I'm hoping to take the expertise that I gained in the microfluidics design process to my own research," he said. Hunt is working in the lab of Sarah Heilshorn, PhD,an associate professor of materials science and engineering.

Those are exactly the kinds of results Fordyce had hoped for.

"This year **See TRAPTASIA, page 5**

Stanford Medicine magazine reports on the future of vision

By Rosanne Spector

Many of the strategies being explored at the School of Medicine to protect, improve and restore vision sound seriously sci-fi. Among them: cornea transplants conducted with magnetic fields instead of scalpels, virtual reality workouts to repair damaged retinas, and bionic vision.

The new issue of *Stanford Medicine* magazine, a theme issue on eyes and vision, includes details about these projects and others pushing the boundaries of biology and technology to help people see.

"Studies show that when it comes to their health, the thing people most worry about, after death, is losing their vision," said Jeffrey Goldberg, MD, professor and chair of ophthalmology, in the report's lead article. "People's productivity and their activities of daily life hinge critically on vision, more than on any other sense."

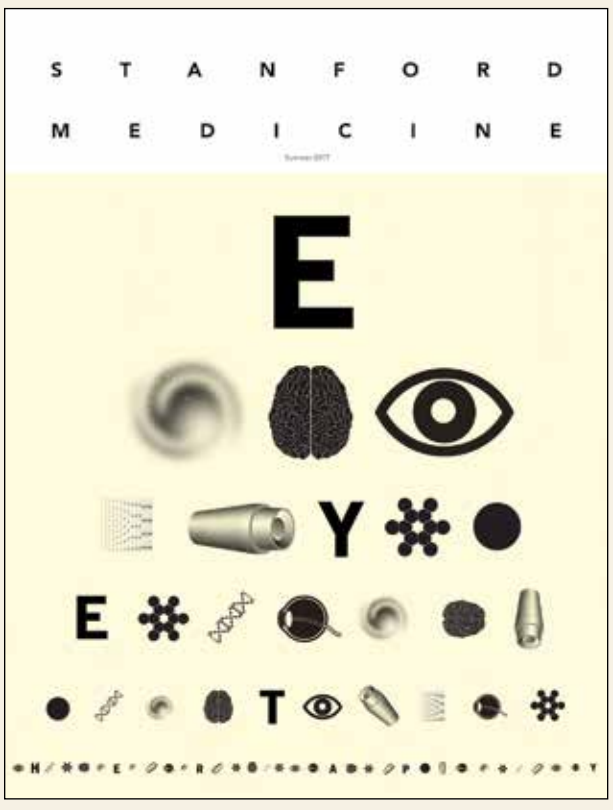
The lead article explains the basic workings of the eye and describes an array of ophthalmological research, including Goldberg's work to repair damaged corneas by injecting healthy cells into the eye and using magnets to pull the cells into position. A patient in a small early study entered the trial legally blind, with 20/200 vision, and left it with 20/40 vision — close to normal. A larger study is planned.

"The fear of vision loss, even for people in lesser stages of disease, can be quite dramatic. So anything we can do to stabilize, better diagnose and hopefully one day restore vision in some of these diseases, I think, will have an enormous global impact," Goldberg said.

Also in the issue, which was produced in collaboration with Stanford's Byers Eye Institute:

- A story about using adaptive optics technology, originally used to track spy satellites, to see inside the eye.
- A feature on progress toward bionic vision — using video glasses and a tiny implant to restore sight.
- A report on using terrifying virtual reality experiences, such as being attacked by sharks, to understand the neuroscience of fear. A video on the subject accompanies the online version of the story.
- An article explaining how neuroscientist Carla Shatz's studies of vision revolutionized the understanding of brain development and continue to uncover surprises, such as interactions between brain cells and the immune system.
- A piece on a mountain-climbing doctor who co-founded the Himalayan Cataract Project, which has performed more than 600,000 cataract surgeries in the developing world.
- A story about removing a tumor from a teen's eye, which not only restored her vision but changed her life.

The issue also includes an article about Stanford Medicine's inaugural issue of *Health Trends Report*, an annual review and analysis of the health care sector. Lloyd Minor, MD, dean of the School of Medicine, explains in the article: "In publishing this report, we hope to show how big data is the most important trend facing the sector and, in the process, inform and educate the entire medical community — including patients, doctors, the private and public sectors — who are actively shaping the future of health care."



Additional stories include a feature on the use of the anesthetic drug ketamine to treat obsessive-compulsive disorder; and an essay by bestselling author Joyce Maynard about living through a loved one's painful death from pancreatic cancer.

The magazine is available online at http://stanmed.stanford.edu. Print copies are being sent to subscribers. Others can request a copy at 723-6911. **ISM**

Hadza of Tanzania experience seasonal variation in gut-microbe diversity

By Bruce Goldman

More evidence that our intestinal microbes are profoundly influenced by the foods we eat — or don't: The gut ecosystems of members of a small group of hunter-gatherers inhabiting Tanzania's Rift Valley show a strong cyclicality consistent with the population's seasonally changing diet.

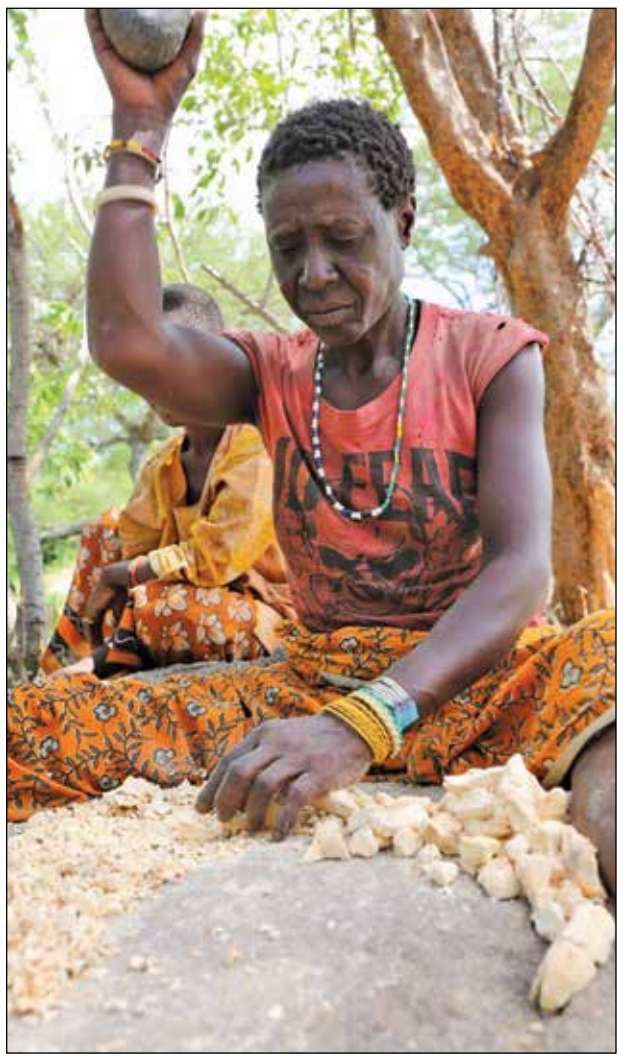
A study led by researchers at the School of Medicine is the first to look at seasonal variations in the gut-microbial composition, or microbiota, of the Hadza, one of the world's few remaining traditional hunter-gatherer populations. The research confirms that the Hadza microbiota is more diverse than, and substantially different from, that of industrialized countries' urban-dwelling denizens.

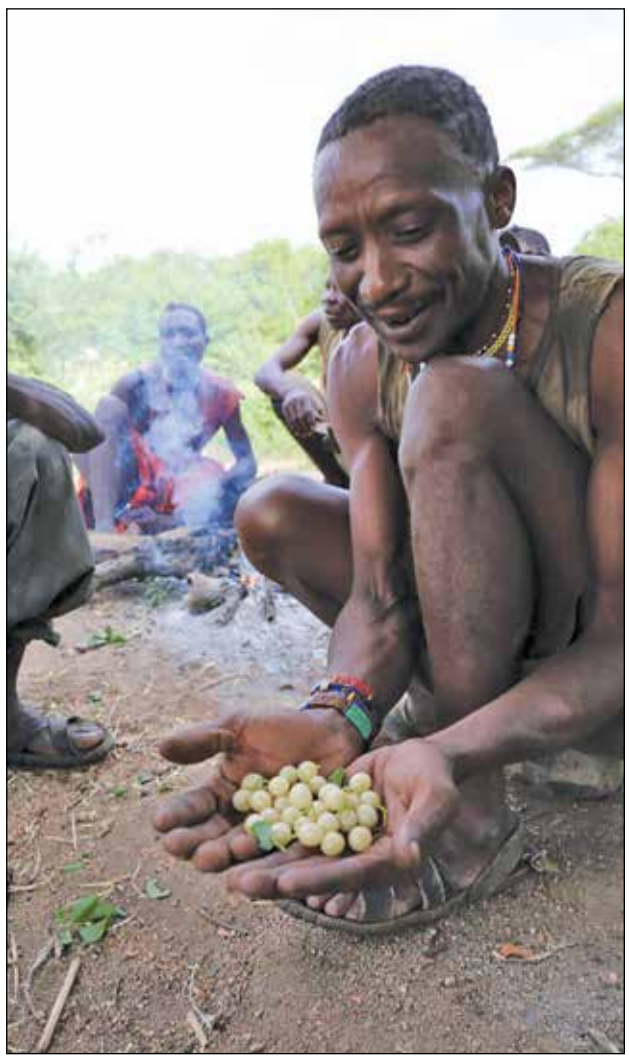
The study is also the first to show that the microbiota of the Hadza population varies seasonally, and that this variation corresponds to their seasonally fluctuating dietary intake. And the research suggests that sweeping changes in the average person's diet over the past 10,000 years could be the key driver in the loss of microbial diversity in the typical modern gut.

"Surviving hunter-gatherer populations are the closest available proxy to a time machine we in the modern industrialized world can climb into to learn about the ways of our remote human ancestors," said Justin Sonnenburg, PhD, associate professor of microbiology and immunology at Stanford.

Sonnenburg is the senior author of the multi-institution study, published Aug. 25 in *Science*. Lead authorship is shared by Sonnenburg's former graduate student Samuel Smits, PhD, and Jeff Leach, director of the Human Food Project in Terlingua, Texas.

JEFF LEACH





(Clockwise from above) A Hadza woman crushes seeds of the baobab tree. Meat plays a larger role in the Hadza diet during the dry season than it does in the wet season. During the rainy season, berries are an important source of food for the Hadza.

The life inside our guts

For more than 15 million years, human beings have co-evolved with thousands of microbial species that take up residence in the lowermost part of the intestine, earning their keep by helping us digest food components we're unable to break down by ourselves, chiefly dietary fiber; manufacturing vitamins and other health-enhancing molecules; training our immune system and fostering the maturation of cells in our gut; and guarding our intestinal turf against the intrusion of all-too-eager competing microbial species, including pathogens.

The advent of agriculture about 10,000 to 15,000 years ago has radically altered our diet. In the past century alone, the typical person's lifestyle has undergone further vast alterations: labor-saving devices' encouragement of a sedentary existence, the introduction of antibiotics and of birth by cesarean section, and the gradual supplanting of fiber-filled whole grains, fruits and vegetables by increasingly processed and fiber-free foods.

These environmental changes have wrought corresponding shifts in our microbial exposures, and in our intestines' ability to serve as hospitable hosts for these symbionts. But it's been hard to apportion the relative contributions of technological and societal innovations to the loss of microbial diversity in modern populations.

STEVE FISCH

Justin Sonnenburg is the senior author of a study about the gut-microbial composition of a hunter-gatherer population in Tanzania.

The new study adds evidence that diet is a major factor.

The Hadza number just over 1,000 people, fewer than 200 of whom adhere to the traditional hunter-gatherer lifestyle, which includes a diet composed mainly of five items: meat, berries, baobab (a fruit), tubers and honey. While Western diets are pretty much the same throughout the year, the Hadza lifestyle doesn't include refrigerators and supermarkets. So the population's diet fluctuates according to the season, of which there are two in the Rift Valley: dry, when meat, baobab and tuber consumption play a relatively larger role; and wet, during which berries, tubers, honey and baobabs prevail. (Tubers and baobab are available year-around.)

"The 100 to 200 Hadza sticking to this routine will possibly lose it in a decade or two, maybe sooner. Some are using cell phones now," Sonnenburg said. "We wanted to take advantage of this rapidly closing window to explore our vanishing microbiota."

Tracking the variation

The investigators collected 350 stool samples from 188 separate Hadza individuals over a roughly one-year period encompassing a bit more than one full seasonal cycle. A thorough analysis of the samples' microbial contents revealed that the gut microbiota varied seasonally, in harmony with the Hadza dietary intake. In particular, a subset of microbial species' populations diminished in the wet season, when honey accounted for a significant portion of caloric intake, and rebounded in the dry season, when consumption of fiber-rich tubers peaked.

That made sense, Sonnenburg said. "Our own microbiota can change significantly from day to day, or even within hours, in response to what we've been eating."

Samples collected during the same season, but a year apart, contained essentially identical microbial populations, indicating resilience to transitory dietary disruptions.

More surprisingly, the bacterial species whose numbers diminish to sub-detectable levels in the wet season, only to bounce back robustly in the next dry season, appear to be the same ones that — although shared by hunter-gatherers in locations as diverse as modern-day Africa and South America — are resoundingly absent in the guts of the vast majority of those who populate the industrialized world.

This observed seasonal cyclicality, in combination with results of a previous study led by two of the study's co-authors, offers a possible hint about the case of the missing microbes.

A 2016 study, published in *Nature* and led by Sonnenburg and senior research scientist Erica Sonnenburg, PhD, showed that while depriving mice of dietary fiber greatly reduced their gut-microbial species diversity, this diversity was restored when the dietary-fiber restriction was lifted. But if this fiber deprivation was maintained for four generations, microbial species that had initially bounced back robustly became permanently lost.

Could this be happening, or could it have already happened, in us?

"Fiber's all that's left at the very end of our digestive tract where these microbes live, so they've evolved to be very good at digesting it," said Sonnenburg. "The Hadza get 100 or more grams of fiber a day in their food, on average. We average 15 grams per day."

In addition to the Sonnenburgs, Stanford co-authors include graduate student Carlos Gonzalez; former graduate student Joshua Lichtman, PhD; and Joshua Elias, PhD, assistant professor of chemical and systems biology.

Researchers from the Lawson Health Research Institute and Western University in Ontario, Canada, the University of California at San Diego, the National Institute for Medical Research in Tanzania, and the New York University School of Medicine also contributed to the study.

The study was funded by the National Institute of Diabetes and Digestive and Kidney Diseases, the Emch Family Foundation, the Forrest & Frances Lattner Foundation, the C&D Research Fund and the Discovery Innovation Fund.

Stanford's Department of Microbiology and Immunology also supported the work. ISM

Traptasia

continued from page 4

was successful beyond my dreams, and the reason is that the students in the course were incredibly creative and talented and driven," Fordyce said. She also credits her graduate student and teaching assistant Kara Brower, who won a teaching award for her efforts. "She went way above and beyond what would be required of a TA and really helped imagine and develop the course," Fordyce said.

"If you put this forward as a model for people at other schools, that could actually make a difference," both for students and the labs that could benefit from microfluidics, she said.

Fordyce and Pringle are also members of Stanford Bio-X. ISM

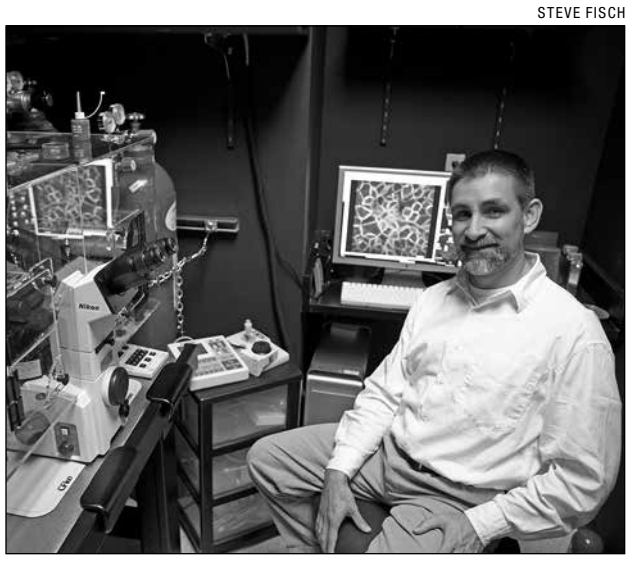
Falkow

continued from page 1

"He would come in and tell all these amazing stories about microbes," Amieva continued. "And he would say, 'You know, I am on the side of the microbes.'"

Amieva joined Falkow's lab as a postdoc after earning an MD and a PhD in cancer biology and completing a pediatrics residency and a fellowship in infectious diseases. "I realized that a lot of the best science comes from making connections between fields or looking at the same thing from a different focal point," he said. During his postdoctoral training, he studied the relationship of *Helicobacter pylori* to its human hosts. "It had just been discovered that it had these little microneedles, and it injected a protein into the host cells, and it seemed like a form of communication between the bacteria and the host," Amieva said. "That injection system and the protein were associated with cancer, so that kind of sold the project for me. But I was a little hesitant because I'm a pediatrician; this is a disease of adults."

STEVE FISCH



Manuel Amieva joined Falkow's lab as a postdoctoral scholar. Now, he's an associate professor of pediatrics and of microbiology and immunology at Stanford.

Soon enough, Amieva found himself on the side of the microbe. "As I started to study it, I realized that this is a pediatric infection," he said. "We acquire it in childhood, and we really don't know much about this interaction until some people get sick later on. And then I started realizing, 'Oh, it's been in humans since humans began.' So it's one of those few microbes that have really coevolved with humans. The more I think about it, it's the perfect microbe to study. It's part of our normal microbiota, and it has some beneficial aspects, but it can turn nasty and lead to cancer, so it is in this balance between being a pathogen and being a commensal," or symbiotic, organism, Amieva said. "And Stanley's always asking these kinds of philosophical questions, like 'What's a pathogen?' I've been trying to figure that out for *H. pylori* since I was in his lab, and I think that's led to a lot of adventures for my students."

Falkow said, "Manuel and I share a great love of teaching. He mentors one-on-one and is very hands-on. And he is an exquisite teacher. To see him in a classroom is to understand seeing somebody at the center of their being."

Amieva and his colleagues have revamped the microbiology course in which he and Falkow's paths first crossed. "We made it a very modern flipped classroom, where students watch videos at home and then they come and do activities," Amieva said. "Stanley is now one of our best facilitators. He'll come and tell some story, like when he put poop in pills for patients before they went into the hospital [at Walter Reed], to prevent diarrhea — essentially, he started doing fecal transplants and got fired for it. Students love it."

Monack also makes sure Falkow stays in touch with students. His office is right outside hers. "Which I finagled," she said. "He was sitting in some office in someone else's lab and was kind of isolated. I knew if he was here and students had to walk through his office, he would like that. He loves it. And they love it. It's perfect."

A 'gentle shove'

It also gives Falkow an up-close view of how Monack mentors her students. "She does what I think is the most important thing: She has an open door," he said. "The student comes and says they want to talk; she drops what she's doing and invites them in if at all possible, closes the door and talks to them as long as they want. I saw her do it today."

Monack and Falkow have been working together in close quarters since 1984, when Falkow hired her, fresh out of college at UC-Davis, as a lab technician. For the next 14 years, Monack managed Falkow's lab and conducted her own research experiments, developing an animal model for pertussis and investigating host cells' proclivity to commit suicide rather than be infected with salmonella.

"We had to learn more and more about the biology of animal cells and human cells, and it was a difficult transition, but we made it," said Falkow. "And in no small measure thanks to her, because she was the common denominator through all these generations of students, and she was the giver of lore to the lab. It got to the point where if you wanted to know something, you asked Denise."

That said, Falkow was concerned about his lab manager's future. "She was able to publish, but she was stuck here, and there was no way for her to advance in the system," he said. "She was basically giving away a lot of her knowledge and her skill to other people."

RYAN MORRIS / NATIONAL SCIENCE & TECHNOLOGY MEDALS FOUNDATION

In 2016, Falkow received the National Medal of Science for his work studying how bacteria can cause human disease and how antibiotic resistance spreads.

It was time for what Falkow called a "gentle shove." As Monack remembered it, "He said, 'You know, Denise, I really think you, in the future, would be happiest if you got your PhD. When I go to the big petri dish in the sky, it's going to be hard for you to find another position where you have the freedom that you're used to, and you might be miserable.' And I thought about this, and I realized, 'He's 100 percent right.'"

During graduate school at Stanford, Monack rotated through several faculty members' labs, ultimately completing her PhD in Falkow's. "I guess I had been brainwashed by then," she said. She accepted a faculty position shortly after Falkow closed his lab in 2005.

Although he is reluctant to use the term "legacy," Falkow will allow that Monack "shares something with me, and I'm very grateful for that." And yet, he emphasizes, she has carried on her work investigating host-pathogen relationships with her own style. "She has her own personality of science," he said. "It's everything that you look for in a student that you train. You don't want them to be clones of yourself — I don't — it doesn't behoove you. And she's turning out students who are in their own right successful, and she takes great joy in their success."

David Relman

That, Monack said, is something she learned from her mentor. "I do think I've modeled my managing style after Stanley's, and it clearly has worked for him. I give graduate students and postdocs a lot of freedom, but I monitor what they're doing, and if they're struggling, I help them. I think it's best to allow people to be creative on their own. You get the best out of people when you make it clear that you trust them and you respect them."

Curiosity and intuition

Relman was a postdoc in Falkow's lab for 5½ years, until a faculty position opened up in the Division of Infectious Diseases. "Stanley always used to say he would have to take out adoption papers, because this was getting to be a bit long," Relman said. It was a joke, but the familial regard was authentic. "He was warm and direct and funny and genuinely interested in me and in his people and in his role as a mentor," Relman said. "But I realized that he didn't view that relationship as a hierarchical one at all. It was his creation of an extended community with a familylike feel."

Relman found the gateway to much of his life's work one day when he and Falkow attended the weekly clinical conference of the infectious diseases division. The presenter was Lucy Tompkins, MD, PhD, the Lucy Becker Professor in Medicine and professor of microbiology and immunology. (She's a Falkow lab alumna herself, and now his wife.)

"She was presenting an interesting case of a disease that clearly seemed to be caused by a bacterium, but no one had been able to grow this organism, and because of that, no one knew what it was, and the usual kinds of testings were all negative," Relman remembered. "So Stanley said, listening and looking at these clumps of bacteria sitting in the spleen or liver, 'There's got to be a way to identify these things that doesn't involve trying to cultivate them.' So I said, 'Well, I'm interested.'"

With a couple of well-placed hunches from Falkow, Relman soon found himself collaborating with microbiologists in Indiana who had found a way to reveal the nature of bacteria in soil without cultivating them, and with scientists in the East Bay, one of whom had just invented the polymerase chain reaction technique to amplify DNA. Using a new experimental approach, Relman and his colleagues identified the bacterium, now classified as a Bartonella, that causes the disease, bacillary angiomatosis. It turned out also to cause cat-scratch disease.

"It was just because of Stanley's curiosity, his willingness to put himself in someone else's world and think hard about their problem, and then as is often the case with Stanley, he has an idea of where the right direction might be," Relman said. "He might not know the details of how to get it done, but he knows, 'Head in that direction; you'll see something that way.' I have since then found myself and maybe deliberately put myself in the position of being one of relatively few clinicians working in an area of science that is mostly populated by nonclinicians, but who have an interest in understanding the clinical ramifications of the story."

Relman used the same method on other diseases, and he ended up using it to look at commensals in the human body. Today, that microbiome research is his main focus.

"That event led to my beginning to do this work on the human microbiome, and that was clearly influenced by Stanley's worldview," said Relman, who is now the Thomas C. and Joan M. Merigan Professor. "He'd always been interested in commensals, although nobody was studying them, but also promoted the general value of curiosity and exploration and risk-taking. I think I pursued all of that work on the microbiome because of him, and about 15 years ago that became the only thing I did."

Falkow is impressed by Relman's ability to collaborate broadly. "David is in full command of at least a cruiser, if not a battleship," he said. "He walks two lines of infectious diseases and basic science, and a lot of people who don't know him wonder at that. I don't know how he handles that many students. That's the amazing thing to me."

The admiration, of course, is mutual. Falkow's mentoring legacy "is exactly the kind of contribution that has a much longer-lasting impact than any particular finding," Relman said. "With the pace of science, there is no paper, no matter how important, that will have continuing impact in the way that a subsequent generation of people will, who if trained especially well or potently, or with sufficient power of influence, will in turn bestow that upon their trainees. There are second- and third-generation Stanley people now who recognize Stanley's contribution to the way in which they do science as not via direct means but by vertical inheritance. I think all of us can only dream to have the kind of influence the way Stanley has had."

'A microcosm of my life'

When Falkow looks at the careers of Amieva, Monack and Relman, he sees, "more or less, a microcosm of my life." Each, he said, has a segment of his personality. "If David is Darwin walking around the Galapagos measuring beaks, Manuel is Darwin walking around the Galapagos enjoying the beauty of the situation," he said. "Denise is more of a generalist and she's moving into immunology — places I didn't go. She's a very practical, pragmatic person.

"When it all comes down to it, when the four of us — or any group of us — are together, we're talking about science," he said. "And the science is the most fascinating part of it." **ISM**

Mouse

continued from page 1

Wu shares senior authorship of the research, which was published Aug. 22 in *Cell Reports*, with Dale Greiner, PhD, professor in the Program in Molecular Medicine at the University of Massachusetts Medical School, and Leonard Shultz, PhD, professor at the Jackson Laboratory. Former postdoctoral scholars Nigel Kooreman, MD, and Patricia de Almeida, PhD, and graduate student Jonathan Stack, DVM, share lead authorship of the study.

"Although these mice are fully functional in their immune response to HIV infection or after transplantation of other tissues, they are unable to completely reject the stem cells," said Kooreman. "Understanding why this is, and whether we can overcome this deficiency, is a critical step in advancing stem cell therapies in humans."

"Humanized mice are critical preclinical models in many biomedical fields helping to bring basic science into the clinic, but as this work shows, it is critical to frame the question properly," said Greiner. "Multiple laboratories remain committed to advancing our understanding and enhancing the function of engrafted human immune systems."

Greiner and Shultz helped to pioneer the use of humanized mice in the 1990s to model human diseases and they provided the mice used in the study.

Understanding stem cell transplants

The researchers were studying pluripotent stem cells, which can become any tissue in the body. They tested the animals' immune response to human embryonic stem cells, which are naturally pluripotent, and to induced pluripotent stem cells. Although iPS cells can be made from a patient's own tissues, future clinical applications will likely rely on pre-screened, FDA-approved banks of stem cell-derived products developed for specific clinical situations, such as heart muscle cells to repair tissue damaged by a heart attack, or endothelial cells to stimulate new blood vessel growth. Unlike patient-specific iPS cells, these cells would be reliable and immediately available for clinical use. But because they won't genetically match each patient, it's likely that they would be rejected without giving the recipients immunosuppressive drugs.

Humanized mice were first developed in the 1980s. Researchers genetically engineered the mice to be unable to develop their own immune system. They then used human immune and bone marrow precursor cells to reconstitute the animals' immune system. Over the years subsequent studies have shown that the human immune cells survive better when fragments of the human thymus and liver are also implanted into the animals.

> "Each roadblock we identify will only serve as a landmark as we navigate the future."

Kooreman and his colleagues found that two varieties of humanized mice were unable to completely reject unrelated human embryonic stem cells or iPS cells, despite the fact that some human immune cells homed to and were active in the transplanted stem cell grafts. In some cases, the cells not only thrived, but grew rapidly to form cancers called teratomas. In contrast, mice with unaltered immune systems quickly dispatched both forms of human pluripotent stem cells.

The researchers obtained similar results when they transplanted endothelial cells derived from the pluripotent stem cells.

A new mouse model

To understand more about what was happening, Kooreman and his colleagues created a new mouse model similar to the humanized mice. Instead of reconstituting the animals' nonexistent immune systems with human cells, however, they used immune and bone marrow cells from a different strain of mice. They then performed the same set of experiments again.

Unlike the humanized mice, these new mice robustly rejected human pluripotent stem cells as well as mouse stem cells from a genetically mismatched strain of mice. In other words, their newly acquired immune systems appeared to be in much better working order.

Although more research needs to be done to identify the cause of the discrepancy between the two types of animals, the researchers speculate it may have something to do with the complexity of the immune system and the need to further optimize the humanized mouse model to perhaps include other types of cells or signaling molecules. In the meantime, they are warning other researchers of potential pitfalls in using this model to screen for immunosuppressive drugs that could be effective after human stem cell transplants.

"Many in the fields of pluripotent stem cell research and regenerative medicine are pushing the use of the humanized mice to study the human immune response," said Kooreman. "But if we start to make claims using this model, assuming that these cells won't be rejected by patients, it could be worrisome. Our work clearly shows that, although there is some human immune cell activity, these animals don't fully reconstitute the human immune system."

The researchers are hopeful that recent advances may overcome some of the current model's limitations.

"The immune system is highly complex and there still remains much we need to learn," said Shultz. "Each roadblock we identify will only serve as a landmark as we navigate the future. Already, we've seen recent improvements in humanized mouse models that foster enhancement of human immune function."

Wu is a member of Stanford Bio-X, the Stanford Cancer Institute and the Stanford Child Health Research Institute. He is also the Simon H. Stertzer Professor.

Additional Stanford co-authors are former research assistant Raman Nelakanti; former postdoctoral scholars Sebastian Diecke, PhD, and Veronica Sanchez-Freire, PhD; postdoctoral scholar Ning-Yi Shao, MD, PhD; instructor Elena Matsa, PhD; and associate professor of pathology Andrew Connolly, MD, PhD.

The research was funded by the California Institute of Regenerative Medicine, the National Institutes of Health and the Helmsley Charitable Trust.

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

Privacy

continued from page 1

Using the technique, the researchers were able to identify the responsible gene mutations in groups of patients with four rare diseases; pinpoint the likely culprit of a genetic disease in a baby by comparing his DNA with that of his parents; and determine which out of hundreds of patients at two individual medical centers with similar symptoms also shared gene mutations. They did this all while keeping 97 percent or more of the participants' unique genetic information completely hidden from anyone other than the individuals themselves.

"We now have the tools in hand to make certain that genomic discrimination doesn't happen," said Gill Bejerano, PhD, associate professor of developmental biology, of pediatrics and of computer science. "There are ways to simultaneously share and protect this information. Now we can perform powerful genetic analyses while also completely protecting our participants' privacy."

Bejerano shares senior authorship of the research, which was published Aug. 18 in *Science*, with Dan Boneh, PhD, professor of computer science and of electrical engineering. Graduate students Karthik Jagadeesh and David Wu share lead authorship of the study.

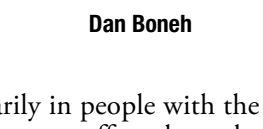
Applying cryptography techniques

The researchers hope that routine implementation of their technique will help individuals overcome any qualms about privacy that may keep them from sharing their genome sequences. In particular, people may be concerned that DNA sequences or genetic variants currently unassociated with diseases may in the future be linked with as-yet-unidentified increases in risk.

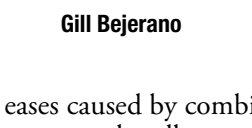
"These are techniques that the cryptography community has been developing for some time," said Boneh, who is the Rajeev Motwani Professor in the School of Engineering. "Now we are applying them to biology. Basically, if you have 1 million people with genomic data they would like to keep private, this approach lets researchers analyze the data in aggregate and only report on findings that are pertinent. An individual might have dozens of anomalous genes, but the researchers and clinicians will only learn about the genes relevant to the study, and nothing else."

When the human genome was fully sequenced in 2001, it was hailed as a remarkable achievement. For the first time, the 3 billion nucleotides that encode the approximately 20,000 genes that keep our bodies running smoothly were tidily listed as a string of letters. But every human has many variations from the published, consensus sequence. These individual differences are what make us unique, but they can also confer increased risk of genetic diseases.

More than 7,000 diseases are caused by variations in the sequence of a single gene. But in order to determine which variations cause the condition, it has been necessary until now to compare the genetic sequences of hundreds or thousands of individuals with and without the disease, letter by letter. Geneticists (or their computer software) then make a list of all the differences and identify which are found primarily in people with the disease under study but rarely in any unaffected people. Those variations are then considered to be prime disease-causing suspects.



Dan Boneh



Gill Bejerano

"There is a general conception that we can only find meaningful differences by surveying the entire genome," said Bejerano. "But these meaningful differences make up only a very tiny proportion of our DNA. There are now amazing tools in computer science and cryptography that allow researchers to pinpoint only these differences while keeping the remainder of the genome completely private."

In 2008, President George W. Bush signed the Genetic Information Nondiscrimination Act, which prohibits discrimination in matters of health insurance and employment based on an individual's genetic information. But there are many other arenas in which such discrimination could potentially occur, including the purchase of life or disability insurance or the application for a loan.

Giving power to the individual

Jagadeesh and Wu worked together to adapt a cryptographic approach known as Yao's protocol and cloud computing for use with human genomes. A key component of the technique is the involvement of the individual whose genome is to be studied. In particular, each individual encrypts their genome (with the help of a simple algorithm on their own computer or smart phone) into a linear series of values describing the presence or absence of the gene variants under study, without revealing any other information about their genetic sequence. The encrypted information is uploaded into the cloud and the researchers then use a secure, multiparty computation (a cryptographic technique that ensures the input data remain private) to conduct the analysis and reveal only those gene variants likely to be pertinent to the investigation.

"In this way, no person or computer, other than the individuals themselves, has access to the complete set of genetic information," said Bejerano. In each case, the analysis was performed within seconds or minutes with moderate computing power. They hope to extend the technique to include diseases caused by combinations of multiple genetic variants or to handle tens of thousands of sequences such as those found in genomewide association studies.

Ultimately the goal is to find the best way to both share the genetic information with researchers while also protecting each patient's privacy in order to advance medical knowledge.

"Often people who have diseases, or those who know that a particular genetic disease runs in their family, are the most reluctant to share their genomic information because they know it could potentially be used against them in some way," said Bejerano. "They are missing out on helping themselves and others by allowing researchers and clinicians to learn from their DNA sequences."

Bejerano is a member of Bio-X, the Stanford Child Health Research Institute, the Stanford Cancer Institute and the Stanford Neurosciences Institute.

Another Stanford study co-author is graduate student Johannes Birgmeier.

The study was funded by Stanford University fellowship grants, the National Science Foundation, the Defense Advanced Research Projects Agency, the David and Lucile Packard Foundation, Microsoft and the Simons foundation.

Stanford's departments of Developmental Biology, of Pediatrics and of Computer Science also supported the work. **ISM**

Med X to focus on promoting positive change in health care

By Tracie White

Medicine X, Stanford's premier conference on emerging health care technology and patient-centered medicine, will return to campus Sept. 15-17.

This year's conference, which will be held at the Li Ka Shing Center for Learning and Knowledge, will focus on the responsibilities of health care citizenship and how individuals can take action to improve health care in the United States.

"Medicine X 2017 will focus on how we can take action to create the change that we want to see in the health care system and move beyond ideas into action," said Lawrence Chu, MD, professor of anesthesiology, perioperative and pain medicine and founder and director of Medicine X. "With the current uncertainty in the future of health care, it's important to stop and consider how each of us might work to create a new culture of caring in health care that doesn't exist right now."

Medicine X aims to bring together everyone who plays a role in health care — researchers, patients, providers, designers, technologists and policy leaders — and encourage them to work together to build a framework for health care transformation, Chu said. This framework, known as "Everyone Included," is a trademark of Stanford Medicine X and was co-developed with a diverse group of health care stakeholders over the past seven years at the conference.

"In January during President Obama's farewell speech, he talked about how his future role was going to be as a citizen," Chu said. "That inspired me to think about how we, as individuals, might consider this role in terms of health care. We hope this conference will give people both the inspiration and the tools and resources they need to take action and create change."

STANFORD MEDICINE X

Lawrence Chu, founder and director of Stanford Medicine X, speaks at the event in 2016.

Keynote speakers include:

- Amy Edmondson, PhD, professor of leadership and management at the Harvard Business School, who will speak on "The importance of creating psychological safety when a patient is a part of a health care team."
- Ai-jen Poo, a 2014 MacArthur "genius grant" recipient and executive director of the National Domestic Workers Alliance, who will speak on "The new caring majority."
- Hooman Noorchashm, MD, PhD, a cardiothoracic surgeon and activist, who will share the story of his late wife, Amy Reed, MD, PhD, who was harmed during a medical procedure, and the journey they began to change U.S. medical practices.

Conference sessions will include: community organizing and how to create meaningful and lasting change in health care; the challenges of digital health; and a panel session moderated by ProPublica reporter Charles Ornstein on partnering to develop shared resources for cancer patients.

Events over the three-day conference will also feature presentations and panels on a range of topics, including:

- Ideas and experiences from experts in the disability community on what access means to them and a discussion of exploring ways to encourage providers and institutions to go beyond compliance.
- A discussion on the current state of clinical trials and how to move from serving only the needs of researchers to those of patients who participate.
- A device demonstration providing hands-on experience with health care technologies presented by the innovators behind them.

Pre-conference events will take place Sept. 14 from 7:30 a.m. to 5:30 p.m., and will include a day-long summit to explore how technology and patient voices can guide the future of employer-based health benefits programs, and an IDEO design workshop in which ePatients can collaborate with designers, researchers, technologists and health care providers to spark new ideas for improving patient care.

Registration for Medicine X is available online at medicinex.stanford.edu. Pre-conference events require separate registration. **ISM**

OF NOTE

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

RAAG AIRAN, MD, PhD, assistant professor of radiology, has been named the runner-up of the 2017 *Science* & PINS Prize for Neuromodulation. The prize recognizes outstanding research performed during the last three years that is described in an essay. His essay, "Neuromodulation with nanoparticles," appeared in *Science* on Aug. 4.

THEMISTOCLES ASSIMES, MD, PhD, was promoted to associate professor of medicine, effective June 1. He is a cardiologist who conducts human molecular epidemiology studies of traits related to complex cardiovascular disease.

SAMUEL CHESHIER, MD, PhD, assistant professor of neurosurgery, was awarded a $115,000 scholar extension grant for his Ty Louis Campbell Foundation award from St. Baldrick's Foundation, which supports research on childhood cancers. He is working to block a signal expressed on cancer cells that protects them from the immune system, with the goal of targeting pediatric brain tumors.

IRIS GIBBS, MD, was promoted to professor of radiation oncology, effective June 1. She is the associate dean of MD admissions. She specializes in the treatment of central nervous system tumors and in the development of new radiotherapy techniques.

CARLOS GONZALEZ, a graduate student in chemical and systems biology, was named a Gilliam Fellow by the Howard Hughes Medical Institute. The honor recognizes doctoral students with the potential to be leaders in their fields and the desire to support diversity in science. He will receive $46,000 a year for up to three years. In addition, his mentor, Joshua Elias, PhD, assistant professor of chemical and systems biology, will receive training in mentorship.

Raag Airan

Themistocles Assimes

Samuel Cheshier

Iris Gibbs

ANUPAMA NARLA, MD, assistant professor of pediatrics, has received a bridge grant from the American Society of Hematology. The grant provides $150,000 for one year to support blood disease research. Her research examines the pathophysiology of ribosomopathies, with the goal of developing new therapies.

MARLENE RABINOVITCH, MD, the Dwight and Vera Dunlevie Professor in Pediatric Cardiology and a professor of pediatrics, was named an American Heart Association Distinguished Science Lecturer for the AHA meeting in November. The honor recognizes scientists and clinicians who have advanced the understanding of cardiovascular disease and stroke. Her research focuses on supporting lung vascular development to ameliorate the effects of heart failure.

GEORGIOS SKINIOTIS, PhD, was appointed professor of molecular and cellular physiology and of structural biology, effective June 1. His research focuses on the application of cryo-electron microscopy for the 3-D visualization of protein complexes, primarily signaling cell surface receptors, with the goal of understanding how they function.

DARRELL WILSON, MD, professor of pediatrics, in collaboration with David Seftel, MD, of Enable Biosciences, has been awarded a $700,000 grant from JDRF, an organization that funds Type 1 diabetes research. The team plans to develop an ultrasensitive auto-antibody panel for the early detection and treatment of the disease. Wilson's research interests include pediatric endocrinology and the role of technology in the management of diabetes.

CAROLINE YU, a medical student, has received a summer student fellowship from the Parkinson's Foundation and the American Parkinson Disease Association. The $6,000 award will support her work on neuroophthalmic clinical markers for Parkinson's disease with her mentor, Joyce Liao, MD, PhD, associate professor of ophthalmology and of neurology. **ISM**

Carlos Gonzalez

Anupama Narla

Marlene Rabinovitch

Georgios Skiniotis

Darrell Wilson

Caroline Yu

JEREMY BITTERMAN / INTERSTICE ARCHITECTS

A rock's purpose

When the industrialist C. J. Huang funded the construction of Stanford Medicine's Asian Liver Center, a nonprofit focused on reducing the incidence of hepatitis B and liver cancer in Asians, he asked that the building design reflect the cultural traditions of the Asian community. To this end, Stanford worked with feng shui master Jetsun Ma Ho Lynn to provide advice on colors and landscaping elements that would have a healing effect on the center's visitors. So what's the deal with that boulder?

Recently, Ho Lynn explained its mystical purpose: "This volcanic rock is composed of fire, earth and metal elements, and the lichen on its surface represents water and wood elements. Wood is energetically related to the liver and brings forth an enhancing, productive chain of the five elements' spiritual powers to support the goals of the Asian Liver Center's work. The empty space under the roof overhang of the center's entrance was a feng shui variable that could disrupt the flow of chi, vital energy, into the building. Adding the large boulder calls attention to the center's establishing goal with its heavy weight and powerful presence." **ISM**