Surgical residents play hooky to stay healthy

By Tracie White

Surgeons working 80 hours a week tend not to get a lot of time to play around. But on a recent weekday morning, about 30 of them gathered on Alumni Green and, dressed in scrubs with beepers on their hips, spent a few hours jumping, screaming, tying blindfolds over their eyes and playing games.

“It’s a switch from dealing with parathyroid cancer,” said resident Blake Read, MD. He had just finished a memory game that involved hopping across a giant checkerboard and was now heading across the lawn to help lift colleagues through a spiderweb of ropes. He admitted it’s hard to take time away from work — “All of us love to be in the operating room” — but that he made the morning’s activities a priority.

The residents were participating in what was essentially structured playtime: a series of games set up by Adventure Associates as part of the Balance in Life program for surgical residents. The games, designed to build teamwork and trust among colleagues, were set up at different stations across the lawn.

“It’s hard to take time away from work — but that he made the morning’s activities a priority. The residents were participating in what was essentially structured playtime: a series of games set up by Adventure Associates as part of the Balance in Life program for surgical residents. The games, designed to build teamwork and trust among colleagues, were set up at different stations across the lawn.

They are not alone’

“Taking time out for play is essential for these residents as they enter their first years as full-time physicians and regularly face life or death decisions,” said Ralph Greco, MD, one of the founders and director of Balance in Life. The program was founded in 2011 following the suicide of a well-respected former surgical resident, Greg Feldman, MD.

“It can tell you a surgical resident would rather be in the operating room than anywhere else on Earth,” said Greco, former director of the general surgery residency program and the Johnson & Johnon Distinguished Professor in Surgery. “They’re passionate about it. We have to force them to take time out to see the doctor and the dentist for themselves.”

The Balance in Life program has continued to thrive over the years and includes a refrigerator stocked with healthy snacks, weekly group therapy with a psychologist, and a mentoring partnership between junior and senior residents. The residents themselves are active in planning and coordinating group activities.

Study: Re-analyzing trial data can lead to new conclusions

By Krista Conger

As many as one-third of previously published randomized clinical trials could be re-analyzed in ways that modify the conclusions of how many or what types of patients need to be treated, according to a new study by researchers at the School of Medicine.

A culture that fails to encourage data sharing makes such re-analysis of the data extremely rare, the researchers said. They were able to identify only 37 published re-analyses over more than three decades of research. Of these, only five were conducted by researchers who were not associated with the original studies.

This project was launched in the aftermath of a controversial research consent form used in a study by researchers at the School of Medicine. "There is a real need for researchers to provide access to their raw data for others to analyze,” said John Ioannidis, MD, DSc, professor of medicine and director of the Stanford Prevention Research Center. “Without this access, and possibly incentives to perform this work, there is increasing lack of trust in whether the results of published, random-
Optogenetics earns Karl Deisseroth Keio Prize in Medicine

By Amy Adams

Today, optogenetics is a widely accepted technol- 
gy for probing the inner workings of the brain, but a decade ago it was the source of some anxiety for Karl Deisseroth, MD, PhD, who was then an assistant pro-
fessor of bioengineering and of psychiatry and behav-
ioral sciences.

Deisseroth had sunk most of the funds he’d been given to start his lab at Stanford as a crazy idea: that with a little help from proteins found in pond scum, he could turn neurons on and off in living animals, using light. If it didn’t work, he’d be out of funds with no pub-
lished research, and likely looking for a new job.

Luckily, it worked, and has just earned Deisseroth, now the D.H. Chen Professor and aHoward Hughes Medical Institute in-
vestigator, 2014 Keio Medical Science Prize. The prize “recognizes outstanding and creative achievements of researchers in the fields of medicine and life sciences,” according to the Keio University Medical Science Fund website.

Thousands of labs around the world now use opto-
genetics to understand and develop treatments for diseases of the brain and mental health conditions, as well as to better understand the complex wiring of our brains.

Deisseroth described the first step of his success in a seminal paper in 2005, but it was many years and many more academic papers before he could breathe easy. “There was a period of several years when not everyone who tried optogenetics got it working,” Deisseroth said. “There were some people who were skeptical about whether it would be useful, and rightly so because there were a number of problems we still had to solve.”

“Often, it is important to realize how this important was going to be,” said Malenka, the Nancy Friend Pritz-
ker Professor in Psychiatry and the Behavioral Sciences. The idea had been floating around, but recognizing the importance of the channelrhodopsin discovery and making it work.”

Helping patients

Deisseroth believes the most important contribution from optogenetics will be in its role in understanding bi-
ology and behavior, but it will also likely contribute to medical advances.

One example of how optogenetics could point to better therapies came from work in Parkinson’s disease.

Deisseroth and his team used optogenetics to stimulate different components of the brain’s wiring in animals with a version of Parkinson’s. The results indicated a possible connection in a region of the brain that is related to how neurons fire: the thalamus, when stimulated, powerfully reduce symptoms.

Deisseroth went on to say that optogenetics is an example of how truly disruptive ideas can arise, will be utterly cut off from our common scientific journey.”

Deisseroth added, “I thought it would work but wasn’t sure it would quite reach this point.”

Lights on

Many years before Deisseroth began tinkering with optogenetics, Craig Cline, the Nobel Prize winner who co-identified the structure of DNA — had argued that neuroscience needed a tool to control one type of cell in the brain without disturbing others underneath. Such a tool, he said, would give neuroscientists a way of turning particular groups of neurons on and off to learn more about the brain functions.

Decades later, scientists around the world were still discussing possible ways of carrying that vision, and Deisseroth’s was among them. He went on to cull his lab’s approach around proteins called microbial opsins that are found in single-celled organ-
isms. He began with an opsin from green algae (a.k.a. pond scum) called channelrhod-
ospin, discovered by the German scientist Peter Hegemann.

This protein responds to light in a man-
ner that is related to how neurons fire: It forms a channel on the cell surface that opens and allows for the flow of ions into the cell, the nerve, that channel opens when it receives a signal to fire. In the algae, it opens in re-
sponse to light. If channelrhodopsin could be made to do the same thing in a neuron of a living animal it might provide a way of controlling the activity of that neuron using light.

The concept seemed theoretically possible but risky, and indeed getting it to work in living animals took many years. Delivering the required large number of opsins into specific types of cells was hard. But the targetting light deep into the brain, both posed chal-
lenges, and many opsins were initially not well-pro-
duced or tolerated by neurons.

When all the key pieces finally fell into place, the researchers were able to use fiber optics to shine a tiny light onto a group of neurons harboring opsins in living animals, and found that targetting light deep into the brain, both posed chal-
lenges, and many opsins were initially not well-pro-
duced or tolerated by neurons.

Meanwhile, while applied to other causes, the technology also began to provoke debate over whether it might one day be useful in treating conditions affecting the brain.

By 2012, scientists had begun investigating optogenetics in the brain, most notably in the midbrain region of the brain that is related to movement.

The idea was that optogenetics might be useful in patients with Parkinson’s disease, by helping to restore movement.

“The more directed and targeted research becomes, the more likely we are to slow our progress, and the more certain it is that the distant and untraveled realms, where truly disruptive ideas can arise, will be utterly cut off from our common scientific journey,” Deisseroth wrote.

He argued that funding agencies need to not only support fundamental research, but also facilitate the translation of that research into work that can one day help patients.

“This is something that Bio-X does well,” Deisseroth said. “His lab is situated in the Excellence Center, which houses Bio-X, an interdisciplinary institute where scien-
tists from different backgrounds work elbow to elbow. They put people who come from different perspectives within shouting distance of each other so those leaps can happen.”

Bio-X has provided seed funding for a number of optogenetics collaborations and also supports the opto-
genetics core, where scientists can learn how to employ the technology in their own labs.

“It is not enough to support people who are fascinated by pond scum and other obscure topics, Deisseroth ar-
gues, if we are to eventually treat depression, autism, Parkinson’s disease and a host of other complex diseases.”

By Tracie White

Researchers have announced the en-
rollment of the first patient in an in-
ternational, multicenter clinical trial comparing the effectiveness of two dif-
ferent treatments for multivessel coro-
nary artery disease.

Coronary artery disease is the common type of heart disease, affecting millions of people worldwide. The con-
dition is caused by a narrowing or block-
age of the arteries to the heart due to plaque, which restricts blood flow and reduces the amount of oxygen to the heart.

The trial, called FAME 3, is sponsored by the Stanford University School of Medicine. It will compare traditional bypass surgery with a minimally invasive stenting procedure for the treatment of multivessel coronary artery disease. Patients who undergo the stenting procedure will first have the blood pressure and flow in their narrowed arteries measured using a cath-
eter-based sensor. The first patient was enrolled by re-
searchers at the Catharina Hospital in the Netherlands, said William Fearon, MD, associate professor of cardiovascular medicine at Stanford and principal inves-
tigator for the trial.

A total of 1,500 patients are being recruited at 50 sites in the United States and around the world. Stanford is recruiting 50 patients for its portion of the trial. Participants will be randomly assigned to either surgery or the stenting procedure.

“We hope the trial will provide us with critical information to help guide patients with multivessel coronary artery disease who require revascular-
ization,” Fearon said, who was an investigator for the previ-
ous FAME trial.

The traditional method for diagnosing coronary artery disease is called coronary angiography. An angiography involves injecting contrast agent into the coronary arteries and performing an X-ray. When multiple coronary narrow-
ings are detected, coronary artery bypass surgery is generally recommended to re-
ster blood flow to the heart. It is one of the most commonly performed surgeries in the United States.

Previous studies have found that patients with multivessel coronary artery disease who undergo stenting procedures based on an angiogram have poorer out-
comes than those who have undergone sur-
ery, Fearon said. One reason for this is that angio-
graphy yields a subjective visual assessment rather than an objective physiological measurement of blockage severity, he said. But such a measurement can be ob-
fuscated by things such as the lighting and the exper-
rater variability.

This new trial will go beyond the traditional stenting method of relying solely on the angiogram to determine which arteries should be stented,” Fearon said. “It will involve insert-
ing a pressure guiding wire into the coronary artery to perform a more in-
depth measurement of blood flow in the vessels to the heart.”

Fearon added that the FAME 3 trial will test the latest generation of drug-eluting stents, which have been shown to perform better than earlier versions.

Results from the previous two FAME trials indicated that relying on an angiogram alone may not be sufficient to accurately guide the procedure.

By Amy Adams is the director of interdisciplinary life science communications for Stanford.
Biodesign fellows develop a device for relieving night terrors

By Emily Hite

Night terrors, a sleep disorder affecting mostly young children, do not pose a serious health threat and typically subside with age. But for the parents of kids who experience them, much sleep can be lost in the meantime.

That’s what Andy Rink, MD, observed when he visited family members last year and woke up to a 3-year-old relative’s nightly screams. The exhaustion the child’s parents faced from months of disrupted sleep took a toll on their daytime functioning.

Rink and Boriah have developed a device that uses precisely timed vibrations to get children suffering from sleep terrors into a healthy sleep pattern. It is about the size of a laptop and is placed under the mattress.

The physician and the engineer are working with School of Medicine sleep researchers Christian Guilleminault and Varun Boriah, who have a specific interest in childhood sleep disorders, have worked closely with Rink and Boriah, provided clinical expertise to the team and are the principal investigators for the study.

Guilleminault and Sullivan won faculty mentor awards from the Biodesign Program for their research and guidance on this project.

Boriah said the Biodesign Program has provided valuable access to the clinic reality.

“Rink said as a fellow, he’s been “exposed to a side you don’t see in a hospital.”

Each year, Biodesign, which is part of the university’s interdisciplinary Bio-X institute, selects 12 applicants for 10-month fellowships in medical device innovation. Biodesign fellows work in teams of two or four. Each fellow flag about 50 observed clinical needs while shadowing healthcare workers for four to six weeks. Then, each team considers the 100 to 200 — or more — needs that have been identified and eliminates all but one during four to five rounds of cutting. (Rink added that the process is “more off-script than that,” and each team’s timeline is different.)

Once a team has focused on a clinical need, they “flame out,” brainstorming “tens of hundreds of ideas for solutions” and “letting the ways of doing it compete,” Boriah said. The teams attempt to solve — in a novel, data-supported way — a healthcare problem that may affect patients or providers, or drive down costs or improve the efficiency of healthcare delivery. The fellows have access to faculty mentors across the Stanford campus and outside experts who provide advice to the teams.

Rink and Boriah had their Biodesign fellowships extended through mid-September — fellows normally leave the program in June — based on the promising nature of their project. They also have been accepted into StarX, a start-up accelerator program in Palo Alto for Stanford-affiliated entrepreneurs, where they are continuing their project.

The ultimate goal, they say, is to help millions of kids, and their parents, get a more peaceful night’s rest.

Emily Hite is a former social media producer in the medical school’s Office of Communication & Public Affairs.

Lab will aim to find out what makes for long, healthy lives

By Becky Bach

The Stanford Prevention Research Center plans to launch the Wellness Living Laboratory, an effort to determine which lifestyle and environmental factors — such as diet, exercise and mental well-being — lead to long, healthy lives.

The laboratory also will examine health interventions such as classes and counseling.

“We need to understand lifestyle choices not just one patient at a time,” said John Ioannidis, MD, DSc, director of the Stanford Prevention Research Center and the C.F. Rehnborg Professor.

The program, abbreviated WELL, is being funded by an unrestricted $10 million gift from Amway’s Nutrilite Health Foundation.

WELL plans to enroll thousands of volunteers — who Ioannidis calls “citizen scientists” — in two initial locations: Santa Clara County, Calif., and China, with plans to expand to other sites in the future.

Researchers launched preliminary work this month and hope to begin enrolling participants this fall.

As currently designed, the program will allow participants to choose which health factors to track and which practices to test for their effect on health.

Cutting-edge sensors and tools will allow participants to report most of their information digitally and remotely, Ioannidis said.

The participants also will have the opportunity to enroll in a variety of clinical trials to test various interventions, such as nutrition counseling or smoking cessation programs, he said.

The program will focus on wellness, rather than diseases.

The hypothesis is that promoting wellness thrwarts diseases, Ioannidis said.

Anyone interested in the work will have the opportunity to benefit from access to a program-wide social networking effort that will include news of successful practices, Ioannidis said.

“This outer sphere could reach out to tens of millions of people,” he added.

Although the project has an initial five-year time frame, Ioannidis said he hopes it will continue for many decades in the future to provide long-term insights.

“There’s clearly a lot of enthusiasm for obtaining clear information about healthy living,” he said.

Ioannidis said researchers selected China because of its large population, rapidly expanding economy and its concomitant growth of chronic disease.

Becky Bach is a science-writing intern for the medical school’s Office of Communication & Public Affairs.

Weis at helm of Structural Biology Department

By Bruce Goldman

William Weis, PhD, the William M. Hoge Professor and director of the School of Medicine’s Bio-X program, has been appointed chair of the Department of Structural Biology. He replaces Joseph Puglisi, PhD, professor of structural biology, who stepped down Sept. 1 after leading the department for 10 years.

“With two Nobel Prize winners on its faculty, four National Academy of Sciences members and three Royal Society members, the Department of Structural Biology is a globally acknowledged powerhouse. That’s no small part due to Jody’s efforts,” said Lloyd Minor, MD, dean of the School of Medicine. “Bill’s record of impressive accomplishments and contributions to multiple areas of research makes him ideally suited to moving the department even further forward.”

Weis holds professorships in structural biology and molecular and cellular physiology. He is also professor and chair of photon science at the SLAC National Accelerator Laboratory.

“Bill is an outstanding scientist, one of the best X-ray crystallographers in the world,” Puglisi said. “He combines a deep knowledge of the underlying biology in the complex systems he investigates. He is organized, widely respected, committed to our department and has a vision for where structural biology needs to go. He will be a fantastic chair.”

Weis earned a PhD at Harvard in 1988. He completed postdoctoral fellowships at Yale under Axel Brunger, PhD, who now chairs Stanford’s Department of Molecular and Cellular Physiology, and at Columbia. Weis joined Stanford’s faculty in 1993 as an assistant professor of structural biology and was promoted to associate professor in 1999.

In 2004, Weis was awarded full professorships in structural biology, molecular and cellular physiology and photon science.

Weis credited his predecessor for maintaining a high standard of departmental excellence.

“Jody brought our department into important areas of biological spectroscopy, and he strengthened our very strong expertise in X-ray crystallography and computational methods,” Weis said. “I am anxious to expand further our department’s breadth by moving us into new areas of molecular and cellular structure and function, and furthering connections with the SLAC National Accelerator Laboratory.”

For more information, visit http://clinicaltrials.gov/ct2/show/CT02100722?term=FAME+3&rank=1.
By Ruth Schechter

A.J. Barker might not have a long commute to work in the morning, but he probably has one of the highest. Each weekday, he climbs 200 feet of steel to position himself in the cab of one of the two enormous, yellow tower cranes at the Lucile Packard Children's Hospital Stanford expansion work site. He then spends the next eight or nine hours "flying iron" — moving steel girders and beams throughout the construction site and helping to assemble the framework of the new state-of-the-art center for pediatric and obstetric care.

Sitting almost 16 stories in the air, Barker uses two handheld joysticks to maneuver the crane's 267-foot working arm, or jib, into position, lowering a hook or coupling it into place, coordinating the connection, and then moving the object to the desired location — all while keeping an eye on the activity on the ground, other cranes, the direction of the wind, even the arrivals and departures of the hospital's Life Flight helicopter.

"I have the coolest office view, and it changes all the time," said Barker, who is working with a subcontractor to DPR Construction, the firm overseeing the expansion project. He is one of the more than 200 contractors, subcontractors, architects and trade specialists working on the hospital's 521,000-square-foot addition. There will be 7,900 tons of steel in the entire superstructure when complete.

Scheduled to open in early 2017, the expansion will add more beds, private rooms, state-of-the-art operating suites, family-friendly amenities and the flexible floor space the hospital needs to adapt to new technologies and streamline services. The children's hospital expansion is part of the Stanford University Medical Center Renewal Project, the largest construction project in Palo Alto's history.

Man and machine

Barker is a second-generation crane operator, who learned the ropes by shadowing his father at work. By the time he was 10, he had soaked up the basics. Now, with 13 years of professional experience, Barker is so attuned to the nuances of his equipment that he can maneuver a joystick to pick up a five-gallon bucket, adjust its lid and place it on a table. A computer console displays the weight he is carrying, the trolley location, the degree of swing on the hook and the wind speed, though Barker said he only uses the computer for additional reference, focusing more on the crane and its load.

"It's like driving a car," he said. "Most of it is about feel. It's a matter of making a connection to the movements of the machine. Though the models may be different, the basics remain the same. You have to adjust how it handles, how quickly it responds. You learn to feel what to do and what not to do."

Barker is familiar with the basic laws of physics, adjusting his speed and movements depending on the weight of his load and how far the trolley is positioned on the jib. The closer the load is positioned to the tower, the more weight the crane can lift safely. He needs to compensate his movements when there is a load of 8,000 pounds at the tip of the jib very differently from when there is a maximum load of 22 tons close to the tower. "The trick is to make only movements to control the load," he said.

All channels open

He remains in constant communication with the men on the ground through two-way radios, while a direct phone line to the other crane operator prevents any overlaps of loads between the two massive jibs. Though the jibs are different heights and lengths — Barker's is 267 feet long — the cranes' loads could infringe on the other's perimeter without perfect coordination.

"When the job starts you can see everything. But once the building goes up, you lose visibility, and there are a lot of blind spots," said the 36-year-old father of three. "You have to rely on the guys on the ground to keep everything safe and up to speed. When you're in the blind you depend on the riggers and signalmen."

The signalmen give him explicit details so he knows how heavy a load to expect and where to move the trolley along the jib before he can lower his hooks. While placing gingerbread — smaller I-beams that reinforce a direct phone line to the other crane operator preventing any overlaps of loads between the two massive jibs. Though the jibs are different heights and lengths — Barker's is 267 feet long — the cranes' loads could infringe on the other's perimeter without perfect coordination.

"When the job starts you can see everything. But once the building goes up, you lose visibility, and there are a lot of blind spots," said the 36-year-old father of three. "You have to rely on the guys on the ground to keep everything safe and up to speed. When you're in the blind you depend on the riggers and signalmen."

The signalmen give him explicit details so he knows how heavy a load to expect and where to move the trolley along the jib before he can lower his hooks. While placing gingerbread — smaller I-beams that reinforce the steel framework of the building — Barker responds to a series of nonstop radio instructions:

"Move it up a dog."
"Left easy. Down easy."
"Swing left. Up easy."
"OK, we're working. Down."

"You have to pay attention at all times," he said. "There's no room for error when you are flying iron and sending a load weighing thousands of pounds over to guys who are standing five stories high on beams that are 8 inches wide."

After climbing up to the cabin, Barker starts each shift with a safety inspection of the equipment on the counter-jib behind the cabin, eyeballing the hoist cable for signs of stress, lubricating the moving parts, and checking the tension on the tower sections' bolts and lattice. He'll go over the plans with the signalmen for safety and efficiency, and discuss options for flying the loads. The crane operates in all weather, except in very high wind or lightning storms.

Special connection

For Barker, working on the hospital expansion project is not a typical job site. While he can't see patients through the existing hospital windows, he knows that his crane holds special fascination for little kids, and he makes it a point to wave or blast his horn whenever he sees families looking up at him from Welch Road.

Early next year, when all the structural steel is scheduled to be in place, Barker will move on to his next job, and the two tower cranes will be taken down section by section by smaller mobile cranes.

"I'm proud to be a part of a project that will make such a positive impact on so many children and families," he said.  

Ruth Schechter is a freelance writer.
Farm students enrich life for zoo animals

By Ruthann Richter

Most days, Floyd the giraffe can be found lingering by the rocks near the female giraffe enclosure in a remote corner of his paddock at the San Francisco Zoo. But instead of food, this device dispenses animal poop, which contains important reproductive cues, it might have helped satisfy some of his curiosity about the females that he was trying to see, Garner said. At the enclosure for Harley the kinkajou — their solutions proved ingenious, Garner said. "They all came up with phenomenal ideas — enrichments that work and that Jason and I hadn't thought of," he said. For the lions, the students were inspired by a tidbit they learned from one of the caretakers: The big cats liked to roll in rhino dung, but were quickly bored by the experience. "That was a little goofy for us, so we decided to play around with that idea," said student Jennifer Ren. She and three fellow students worked through a weekend in the School of Engineering's Product Realization Lab to build a contraption they dubbed the Poop Shooter. It's based on a modified fish-feeder, a slow conveyor belt, which Watters had employed for dispensing food at various intervals to the anteaters. But instead of food, this device dispenses animal poop, which is in ready supply at the zoo. At random times throughout the day, it shoots giraffe and oryx pellets into the lions' den, stirring the interest of the normally lethargic cats. "It was amazing," Garner said. "Lions are around all day watching and waiting. But when the zoo put the enrichment in, it was like somebody just flipped a switch. The male lion was up and about and smelling and searching for the giraffe droppings, and performing all of this wonderful lion behavior." "It's based on a modified fish-feeder, a slow conveyor belt, which Watters had employed for dispensing food at various intervals to the anteaters. But instead of food, this device dispenses animal poop, which is in ready supply at the zoo. At random times throughout the day, it shoots giraffe and oryx pellets into the lions' den, stirring the interest of the normally lethargic cats. "It was amazing," Garner said. "Lions are around all day watching and waiting. But when the zoo put the enrichment in, it was like somebody just flipped a switch. The male lion was up and about and smelling and searching for the giraffe droppings, and performing all of this wonderful lion behavior." "It's based on a modified fish-feeder, a slow conveyor belt, which Watters had employed for dispensing food at various intervals to the anteaters. But instead of food, this device dispenses animal poop, which is in ready supply at the zoo. At random times throughout the day, it shoots giraffe and oryx pellets into the lions' den, stirring the interest of the normally lethargic cats. "It was amazing," Garner said. "Lions are around all day watching and waiting. But when the zoo put the enrichment in, it was like somebody just flipped a switch. The male lion was up and about and smelling and searching for the giraffe droppings, and performing all of this wonderful lion behavior." "It's based on a modified fish-feeder, a slow conveyor belt, which Watters had employed for dispensing food at various intervals to the anteaters. But instead of food, this device dispenses animal poop, which is in ready supply at the zoo. At random times throughout the day, it shoots giraffe and oryx pellets into the lions' den, stirring the interest of the normally lethargic cats. "It was amazing," Garner said. "Lions are around all day watching and waiting. But when the zoo put the enrichment in, it was like somebody just flipped a switch. The male lion was up and about and smelling and searching for the giraffe droppings, and performing all of this wonderful lion behavior." "It's based on a modified fish-feeder, a slow conveyor belt, which Watters had employed for dispensing food at various intervals to the anteaters. But instead of food, this device dispenses animal poop, which is in ready supply at the zoo. At random times throughout the day, it shoots giraffe and oryx pellets into the lions' den, stirring the interest of the normally lethargic cats. "It was amazing," Garner said. "Lions are around all day watching and waiting. But when the zoo put the enrichment in, it was like somebody just flipped a switch. The male lion was up and about and smelling and searching for the giraffe droppings, and performing all of this wonderful lion behavior." "It's based on a modified fish-feeder, a slow conveyor belt, which Watters had employed for dispensing food at various intervals to the anteaters. But instead of food, this device dispenses animal poop, which is in ready supply at the zoo. At random times throughout the day, it shoots giraffe and oryx pellets into the lions' den, stirring the interest of the normally lethargic cats. "It was amazing," Garner said. "Lions are around all day watching and waiting. But when the zoo put the enrichment in, it was like somebody just flipped a switch. The male lion was up and about and smelling and searching for the giraffe droppings, and performing all of this wonderful lion behavior." "It's based on a modified fish-feeder, a slow conveyor belt, which Watters had employed for dispensing food at various intervals to the anteaters. But instead of food, this device dispenses animal poop, which is in ready supply at the zoo. At random times throughout the day, it shoots giraffe and oryx pellets into the lions' den, stirring the interest of the normally lethargic cats. "It was amazing," Garner said. "Lions are around all day watching and waiting. But when the zoo put the enrichment in, it was like somebody just flipped a switch. The male lion was up and about and smelling and searching for the giraffe droppings, and performing all of this wonderful lion behavior." For the students, the experience of being involved in a unique project like this was a treat and they were happy to see the benefits it brought to the zoo.
Residents

continued from page 1
bring residents together in a relaxed atmosphere, and to show them most important of all that they are not alone,” said Arghavan Salles, MD, a chief surgical resident who was busy coaching blindfolded colleagues through an obstacle course.

“One thing we think this is kind of holiness,” said Salles, who was one of a group of residents who helped found Balance in Life along with Greco. “But at the end of the day, if we want to have better care for our patients, we need to take care of each other, too.”

She paused to instruct a blindfolded colleague. “Hey, the thing is, surgery is a super critical field,” she continued. “You face constant judgment in this operating room. Everyone is working at the fringes of their abilities. They’re stressed.”

Trend toward wellness programs

In recent years, hospitals, medical schools and residency programs have been making changes to help medical students and residents better cope with stress stemming from the pressure to excel, the constantly increasing amount of information to absorb and the second-time trauma of caring for sick people.

In 2003, work hours were reduced to 80 hours a week from 120 hours a week for residency programs nationwide. A growing number are providing confidential counseling services. At Stanford, several other residency programs in addition to surgery now have wellness programs, including pediatrics and anesthesiology. And this year, the medical school established an Office of Medical Student Wellness.

But promoting wellness — learning how to balance psychological and physical health throughout a career in medicine — holds particular meaning for Stanford’s surgical residency program because of Feldman’s death, Greco said.

“The residency program was just rocked to its knees,” he said. “And it was widely considered a role model and mentor. He died after completing his surgical residency at Stanford and four months into his vascular surgery fellowship at another medical center.

“It was a very frightening time,” Greco said. “Residents were questioning whether they’d made the right choices.”

In the months following the tragedy, Greco and Thomas Krummel, MD, professor and chair of surgery, met every Monday to write down different ideas on a yellow legal pad they had tried to prevent anything like this from happening again.

With the support of Feldman’s family and her surgical residents, the Balance in Life program was born.

Remembering a colleague

Thirty-eight-week pregnant, surgical resident Cara Liebert was carefully maneuvering through the rope web while her teammates giggled. Liebert was a medical student at Stanford when Feldman was a surgical resident.

“He had a lot to do with mentoring me to apply to general surgery residency,” said Liebert, who organized the morning’s event. “I didn’t even know he was struggling.

After several hours, the games would end, and the residents would head back to their jobs. But not before bringing many of their job skills to bear on the games at hand. This was a competitive group and prided itself on doing a job well, said Adventure Associates director Bill Jacocks.

No one slack ed. They furrowed their brows; several bit their nails. Sometimes they barked instructions a bit too loudly to their colleagues: “No, no, no, dude! Go left! Go left!”

Or got a bit too critical: “Oh my god, why are you going so fast?! Take your time!”

But mostly they laughed, took time to breathe in the outdoor air and cheer for one another before heading back to the OR. 

Re-analysis

continued from page 1
ized trials are credible and can be taken at face value. The recent hot debates about whether oseltamivir works are only the tip of the iceberg in this crisis of confidence.

Oseltamivir is an antiviral medication marketed under the trade name Tamiflu. Although it is licensed to treat influenza A and influenza B, some subsequent analyses and trials conducted after the drug was approved have suggested that its benefits do not outweigh the risks or side effects in otherwise healthy adults.

Ioannidis is the senior author of the recent study. Post-doctoral scholar Shunl Ebrahim, PhD, is the lead author. Ioannidis is co-director of the recently launched Meta-Research Innovation Center at Stanford, or METRICS, which aims to advance excellence in scientific research by evaluating and optimizing scientific practices. Enhancing reproducibility and data sharing is a core component of this endeavor.

Searching for data

Ebrahim and his colleagues used the MEDLINE database to conduct their study. MEDLINE is a bibliographic database maintained by the National Library of Medicine. It contains over 25 million citations of biomedical publications from roughly 5,600 journals worldwide. They searched for articles written in English describing the re-analysis of raw data used in previously published studies. Meta-analyses were excluded from the study, as were studies testing a different hypothesis than the original trial.

The researchers screened nearly 3,000 articles of potential interest and read the full text of 226. Of these, 38 were deemed eligible for their study. Two were subsequently excluded because the articles describing the original clinical trials on which they were based were unavailable, and one contained two re-analyses. Of the 37 re-analyses evaluated for the study, 32 had an overlap of at least one author from the original paper.

Thirteen of the re-analyses of the total (35 percent of the total) came to conclusions that differed from those of the original trial with regard to who could benefit from the tested medication or intervention: Three concluded that the patient population to treat should be different than the one recommended by the original study; one concluded that fewer patients should be treated; and nine concluded that more patients should be treated.

The differences between the original trial studies and the re-analyses often occurred because the researchers conducting the re-analyses used different statistical or analytical methods, ways of defining outcomes or ways of handling missing data. Some re-analyses also identified errors in the original trial publication, such as the inclusion of patients who should have been excluded from the study.

Different conclusions

The aims of the re-analyzed studies varied widely. For example, one study on the treatment of enlarged, bleeding veins in the esophagus concluded that sclerotherapy, in which physicians use an endoscope to inject the veins with chemicals to induce blood clots, reduced mortality even though it didn’t prevent rebleeding. The re-analysis, which used a different statistical model of risk, concluded the treatment did prevent rebleeding but didn’t reduce mortality. The new conclusion suggested that the intervention would be best given to patients with rebleeding, rather than those at highest risk of death from the condition.

Another study investigated the best way to deliver a medication to stimulate the production of red blood cells in people with anemia by comparing a fixed dose administered once every three weeks with weight-based weekly dosing.

In the re-analysis, the conclusion changed when investigators used an updated hemoglobin threshold level to determine when therapy should be initiated.

“The high proportion of re-analyses reaching different conclusions than the original papers may be partly an artifact,” said Ioannidis, who also is the C.F. Rehnberg Professor in Disease Prevention. “By that I mean that, in the current environment, re-analyses that reach exactly the same results as the original would have great difficulty getting published. However, making the raw data of trials available for re-analyses is essential not only for re-evaluating whether the original claims were correct, but also for using these data to perform additional analyses of interest and combined analyses.”

In this way, existing raw data could be used to explore new clinical questions, and may sometimes eliminate the need to conduct new trials.

The fact that researchers conducting re-analyses often came to different conclusions doesn’t indicate the original studies were necessarily biased or deliberately falsified, Ioannidis added. Instead, it emphasizes the importance of making the original data freely available to other researchers to encourage dialogue and consensus, and to discourage a culture of scientific research that rewards scientists only for novel or unexpected results.

“I am very much in favor of data sharing, and believe there should be incentives for independent researchers to conduct these kinds of re-analyses,” said Ioannidis. “They can be extremely insightful.”

Other Stanford co-authors of the study are Kristian Thorlund, PhD, and Edward Mills, PhD, visiting associate professors at the Stanford Prevention Research Center.

The research was supported by post-doctoral awards from METRICS, Elevate and SickKids Restramp; the Canadian Institutes of Health Research Canada Chair; and METRICS, which is supported by a grant from the Laura and John Arnold Foundation.

Stanford’s Department of Medicine also supported the work.
The fourth annual Canary Challenge, a fundraising bike ride to support research in early cancer detection, will be held Sept. 27. Proceeds from the event benefit the Canary Center at Stanford for Cancer Early Detection. For information about registering for the ride, volunteering or making a donation, visit http://cancerchallenge.com.

So far, more than 1,000 people have registered to ride, up from 830 last year. The event organizers aim to raise more than $1 million. Stanford students and postdoctoral scholars can register for $25. They must commit to raising at least $100. The regular registration fee is $100, with a minimum fundraising commitment of $400. Stanford employees and other affiliates can save $25 on registration by using the discount code BIKE25.

Riders may join a team, start their own team or register as an individual. They can choose among 5-kilometer, 10-kilometer, 57-kilometer, 75-mile, or 100-mile routes. All rides begin at HP headquarters at 3000 Haven St. in Palo Alto. Riders get complimentary breakfast and lunch, as well as food and water along the routes, mechanical and medical assistance and gift bags.

All riders must meet their fundraising minimum before they can participate. Details are available online at cancer.stanford.edu/training/tumorheterogeneity.

Other events

The panelists are Michele Barry, MD, professor of medicine and director of the Stanford Center for Innovation in Global Health; Doug Owens, MD, professor of medicine and director of the Center for Health Policy at the institute; David Relman, MD, a professor of medicine and of microbiology and immunology; Stephen Stedman, PhD, a senior fellow at the institute and deputy director of the Center on Democracy, Development and the Rule of Law; and Paul Wise, MD, professor of pediatrics.

The event is free and open to the public. No RSVP is necessary. Details are available at stanfordmedicine.org/events/cancerchallenges.
Kidney transplants give Hawaii siblings chance to get growing

By Elizabeth Devitt

There’s one thing that 8-year-old Dominic Faisca, of Hawaii, has always wanted to be: taller.

At only 3-feet-4-inches tall, his growth has been thwarted by a rare, late-onset genetic disease in which an amino acid — cystine — builds up and forms crystals in the kidneys, the cornea of the eye and other places in the body. In the kidneys, these crystals dissolve oxygen and exhaust the stores of the nutrients they need to grow and sometimes lead to renal failure.

But now, with the new donor kidney he received at Lucile Packard Children’s Hospital Stanford in June, Dominic is working on that height thing again.

Only about 10 percent of people in this country who have the disease, said Paul Grimm, MD, medical director of the pediatric kidney transplant program at Lucile Packard Children’s Hospital Stanford, which is the highest-ranking kidney transplant program for children on the West Coast.

In this “recessive” disease, children have to inherit two copies of a faulty gene before cystinosis occurs. As long as there’s one normal gene, there’s no problem.

But when both parents carry a faulty gene (in this case, unknowingly), each child has a 25 percent chance of developing the disease, said Grimm, who is also a professor of pediatric nephrology at the School of Medicine.

That’s because his older sister, Julia, now almost 10, was diagnosed with the disease at 8 months of age. Over the years, doctors cared for the two sisters and collaborated with more than 100 locations in eight states throughout the western United States.

Care teams used medication and nutritional support to keep the Faisca kids’ kidneys functioning for as long as possible before the younger ones were placed on the transplant list.

The first knot in the course of the disease, the accumulated cystine crystals irreparably damage the kidneys. So, when monitoring tests showed that both of Julia’s kidneys were failing, she was placed on the active list in May 2013.

Three months later, she was living with a new donor kidney to replace her two ailing kidneys, thanks to a successful transplant surgery led by Daniella Musgrave, MD, professor of multi-organ transplantation at Stanford. She has since added 7 inches to her petite frame.

Next up was Dominic. Although his name went on the transplant list first, for several months the timing of his transplant was a surprise. The Faisca family had already assembled a plane to Stanford for Julia’s routine, 100-day post-transplant kidney biopsy. During the trip, Dominic was slated to start dialysis for more-intensive kidney support. But their plans changed as soon as they landed in San Jose: a call came that a donor organ was available. Again, it was conception leading the successful surgery.

“We’ve been busy — two Faisca transplants in less than a year,” said the kids’ mom, Natasha. The family draws support from their tight-knit community on the Big Island. But she also relies on the community and care teams at Lucile Packard Children’s Hospital Stanford and Stanford Children’s Health, which are part of Stanford Medicine, and the ongoing nephrology care back in Hawaii.

“Every year in our office is thrilled that Dominic and Julia were able to receive donor kidneys,” said James Mussgrave, MD, the kids’ pediatric nephrologist in Honolulu. “They’re a wonderful family and they’ve been, through a lot, and they’re living proof that organ donation saves lives.”

Dominic is thankful. “Dr. Mussgrave at home and the doctors at Stanford have gone above and beyond anything you would ever imagine. Everyone does everything they can to look after you. It’s all about the kids,” said Natasha.

“And when we have a transplant it’s wonderful to be able to meet other families that are enduring the same things.”

After spending their summer vacation visiting all things Stanford, Dominic and Julia are back in Hawaii now and showing off their growing selves to friends at school.

“Since their transplants, they aren’t picky eaters anymore,” Natasha said. “I joke with the doctors that the kids are eating me out of the house now. But it’s well worth it.

Although they’ll always be on medication to protect their new kidneys and will need to return for twice-yearly checkups at Stanford, there’s finally a sparkle in their eyes, Natasha said. “Dominic and Julia are growing like weeds,” Grimm said, “and it’s really fun to watch them turn into regular kids.”

Elizabeth Devitt is a freelance writer.