INSIDE STANFORD MEDICINE

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Medical students found out March 17 where they would be going for their residencies.

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# Stem cell 'therapy' blinds three patients

By Becky Bach

Three people with macular degeneration were blinded after undergoing an unproven stem cell treatment that was touted as a clinical trial in 2015 at a clinic in Florida. Within a week following the treatment, the patients experienced a variety of complications, including vision loss, detached retinas and hemorrhage. They are now blind.

A paper documenting the cases was published March 16 in *The New England Journal of Medicine*.

The article is a "call to awareness for patients, physicians and regulatory agencies of the risks of this kind of minimally regulated, patient-funded research," said Jeffrey Goldberg, MD, PhD, professor and chair of ophthalmology at the School of Medicine and co-author of the paper.

The three patients — all women, ranging in age from 72 to 88 — suffered from macular degeneration, a common, progressive disease of the retina that leads to loss of vision. Before the surgery, the vision in their eyes ranged from 20/30 to 20/200. Now, the patients are likely to remain blind, said co-author Thomas Albini, MD, an associate professor of clinical ophthalmology at the University of Miami, where two of the patients were subsequently treated for complications from the stem cell treatments. "Although I can't say it's impossible, it's extremely unlikely they would regain vision."

### Appealing to patients 'desperate for care'

Two of the patients learned of the so-called clinical trial on ClinicalTrials.gov, a registry and results database run by the U.S. National Library of Medicine, where it was called "Study to assess the safety and effects of cells injected intravitreal in dry macular degeneration." Some of the patients believed they were participating in a trial, although the consent form and other written materials given to the patients did not mention a trial, Albini said.

"There's a lot of hope for stem cells, and these types of clinics appeal to patients desperate for care who hope that stem cells are going to be the answer, but in this case these women participated in a clinical enterprise that was off-the-charts dangerous," Albini said.

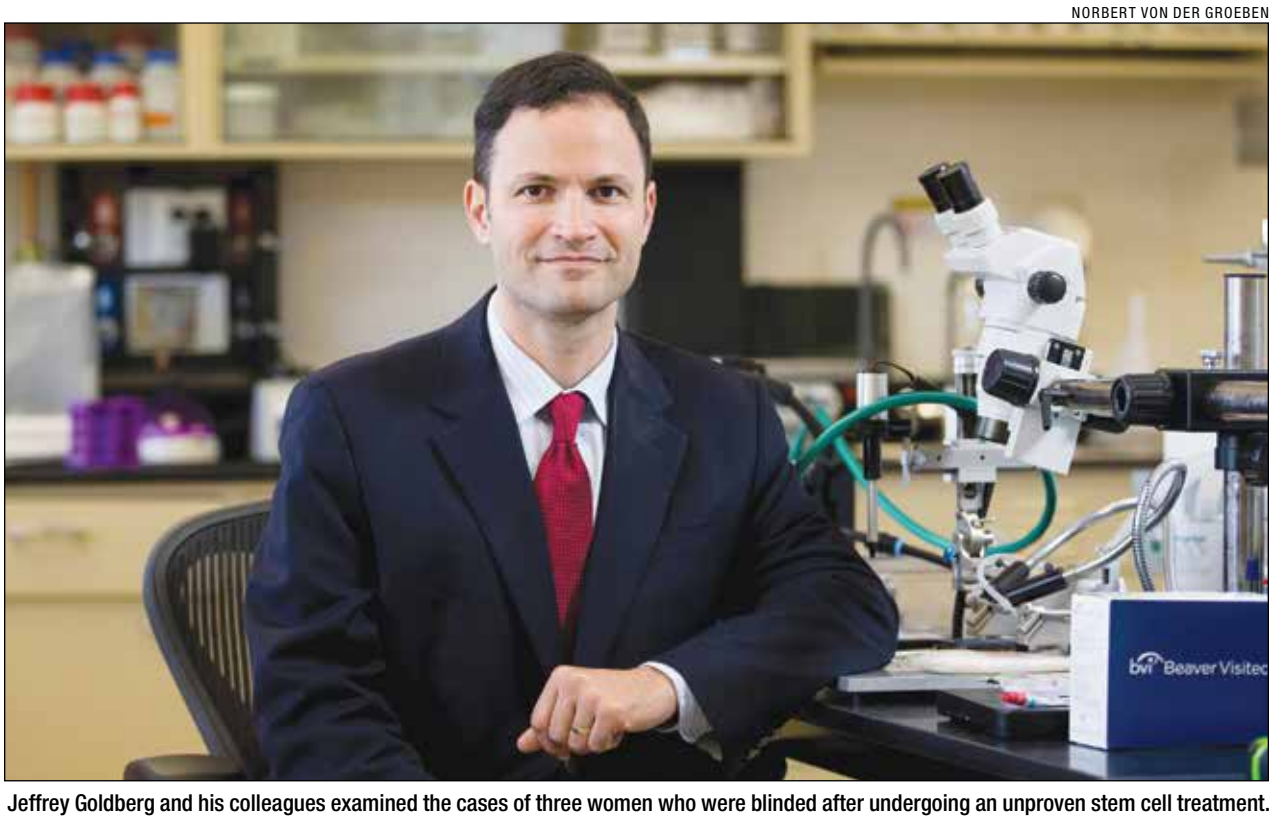
Each patient paid $5,000 for the procedure. Any clinical trial that has a fee should raise a red flag, the authors said.

"I'm not aware of any legitimate research, at least in ophthalmology, that is patient-funded," Albini said.

At the clinic, which is not named in the paper, the patients had fat cells removed from their abdomens and a standard blood draw. The fat tissue was processed with enzymes, with the goal of obtaining stem cells. Platelet-dense plasma was isolated from the blood. The cells were then mixed with the platelet-dense plasma and injected into their eyes. Patients reported that the entire process took less than an hour, Albini said. The patients had both eyes treated at once — another red flag, Albini and Goldberg said, because most doctors would opt for a conservative approach to observe how one eye responds to an experimental treatment before attempting the other eye.

Shoddy stem cell preparation may have led to some of the patients' complications, which could have been caused by injection of a contaminant or the cell wash solution into the eye, Albini said. When injected into the eye, the stem cells also could have changed into myofibroblasts, a type of cell associated with scarring.

NORBERT VON DER GROEBEN



Jeffrey Goldberg and his colleagues examined the cases of three women who were blinded after undergoing an unproven stem cell treatment.

### No evidence of vision restoration

But even if executed correctly, there is no evidence suggesting that the procedure could help restore vision, Goldberg and Albini said. In fact, there is sparse evidence that adipose-derived stem cells, the type of cells that the clinic claimed to use, are capable of differentiating, or maturing, into retinal pigment epithelium or photoreceptor cells, which play a critical role in macular degeneration and are the

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# Initial hospital costs for gunshot wounds just 'tip of the iceberg'

By Devika G. Bansal

Gun violence resulted in initial hospitalization costs of more than $6.6 billion nationwide from 2006 through 2014 — an average of $734.6 million per year, according to a study by researchers at the School of Medicine.

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In an analysis of data from 267,265 patients who were admitted for firearm-related injuries during the nine-year period, the researchers reported that the $6.6 billion figure is only a fraction of the total hospital costs incurred by gunshot wounds: It does not include costs of emergency room visits — medical costs for patients who are treated and released or those who are treated but die before admission — or hospital readmissions.

The study was published online March 21 in the *American Journal of Public Health*. The lead author is medical student Sarabeth Spitzer. The senior author is Thomas Weiser, MD, associate professor of surgery.

"There is a high cost for these injuries, especially because they are preventable," Spitzer said. The study included hospitalization costs of shooting injuries that were self-inflicted, unintentional or due to assault.

### Little research on gun violence

At Stanford, 10 percent of trauma patients are admitted with gunshot or knife wounds — a small but important proportion of the patient population, Weiser said.

Despite the scale of the problem, there exists surprisingly

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# Psychiatrist advised producers on upcoming teen-suicide drama

By Erin Digitale

When Stanford psychiatrist Rona Hu, MD, was invited to help shape the script of a Netflix series about teenage suicide, she knew it would be an unusually good opportunity to communicate with teenagers about mental health issues.

The new series, *13 Reasons Why*, which premieres March 31, is based on a bestselling 2007 novel about a high-school student who dies by suicide after being bullied by her classmates.

The show's producers faced a challenge: They wanted to retain the book's basic plot without romanticizing suicide, since such portrayals can contribute to suicide contagion. Hu agreed to advise them.

"It was a good opportunity to make sure that something about suicide was handled responsibly in the media," said Hu, clinical associate professor of psychiatry and behavioral sciences. "The production team seemed very sincere about wanting to do good and not do harm." Hu has volunteered in suicide-prevention efforts for Palo Alto teenagers, so she was already accustomed to discussing the subject.

Rona Hu

In the novel, *Th1rt3en Reasons Why*, the book's main character, Hannah, records cassette tapes that she arranges to have sent to people who bullied her. Two weeks after her death, they receive the tapes, on which Hannah explains how each of them contributed to her desire to die.

### 'Concerned by a number of things'

"I was concerned by a number of things," Hu said, describing her reactions to the novel. "There are only teenagers in the book; parents are barely mentioned. If teens are contemplating suicide to get back at bullies, they may not realize how much collateral damage they can do to people

See DRAMA, page 7

# Studies of scientific bias targeting the right problems

**By Jennie Dusheck**

In all fields of science, small studies, early studies and highly cited studies consistently overestimate effect size, according to a study led by researchers at the School of Medicine.

A scientist's early career status, isolation from other researchers and involvement in misconduct also appear to be risk factors for unreliable results, the research team reported.

A paper describing the work was published online March 20 in the *Proceedings of the National Academy of Sciences*. The lead author is Stanford senior research scientist Daniele Fanelli, PhD, and the senior author is John Ioannidis MD, DSc, professor of medicine and of health research and policy.

Virtually all scientific work may be afflicted by some kind of bias, Ioannidis said. But how common different kinds of bias are, what factors cause bias, which kinds of bias are most common in different disciplines and how bias can be reduced are all questions being examined by researchers who study how science is done.

"I think that this is a mapping exercise," said Ioannidis. "It maps all the main biases that have been proposed across all 22 scientific disciplines. Now we have a map for each scientific discipline, which biases are important and which have a bigger impact, and therefore scientists can think about where do they want to go next with their field."

To show which sources of scientific bias were most common, the researchers reviewed more than 3,000 meta analyses that included nearly 50,000 individual research studies across 22 scientific fields.

"Our study tested with much greater accuracy than before several hypotheses about the prevalence and causes of bias," said Fanelli. "Our results send a reassuring message, but only in part."

## Types of bias

The researchers examined seven hypothesized kinds of scientific bias:

- Small-study effect: when studies with small sample sizes report large effect sizes.
- Gray literature bias: the tendency of smaller or statistically insignificant effects to be reported in PhD theses, conference proceedings or personal communications rather than in peer-reviewed literature.
- Early-extremes effect: when extreme or controversial findings are published early just because they are astonishing.
- Decline effect: when reports of extreme effects are followed by subsequent reports of reduced effects.
- Citation bias: the larger the effect size, the more likely the study will be cited.
- United States-effect: when U.S. researchers overestimate effect sizes.
- Industry bias: when industry sponsorship and affiliation affect the direction and size of reported effects.

The Stanford team also looked at factors that have been hypothesized to increase the risk of bias, such as size and types of collaborations, the gender of the researchers or pressure to publish.

By far, the greatest bias came from small studies, while other sources of bias had relatively small effects. The team also found that small and highly cited studies and those in peer-reviewed journals seemed more likely to overestimate effects; U.S. studies and early studies seemed to report more-extreme effects; early-career researchers and researchers working in small or long-distance collaborations were more likely to overestimate effect sizes; and, not surprisingly, researchers with a history of misconduct tended to overestimate effect sizes.

On the other hand, studies by highly cited authors who published frequently were not more affected by bias than average. Research by men was no more likely to show bias than that of women. And scientists in countries with very strong incentives to publish, such as the United States, didn't seem to have more bias than studies from countries where the pressure was less. These results confirm, with much greater accuracy, previous studies on retractions and corrections and studies using more indirect proxies of bias.

"A country that has incentives to publish more may also have other features that make its science better," Ioannidis said.

Each kind of bias may result from a variety of mechanisms. For example, in small studies, it's easier to get "statistical significance" if the effect size is large. Since studies with statistically significant results are more likely to be published, it follows that small studies with large effects are also more likely to be published. Even independent of statistical significance, larger effects are more likely to be published than smaller effects.

NORBERT VON DER GROEBEN

John Ioannidis is the senior author of a study that found the biggest single source of bias across all fields of science comes from small-study effects.

Ioannidis said that in the data they examined, the influence of different kinds of bias changed over time and seemed to depend on the individual scientist. "We show that some of the patterns and risk factors seem to be getting worse in intensity over time," he said. "This is particularly driven by the social sciences, so if you broke scientific fields into big bins of biology, medicine, physical sciences and social sciences, it seems that the social sciences are seeing the more prominent worsening of these biases over time."

One of the most unexpected findings of the study, Fanelli said, was that the kinds and amounts of bias were very irregularly distributed across the literature. "Although bias may be worryingly high in specific research areas, it is nonexistent in many others," he said. "So bias does not undermine the scientific enterprise as a whole."

Another finding of the study is that the relative magnitude of biases closely reflects the level of attention that they receive in the literature. That is, the kinds of biases researchers are most concerned about are in fact the ones they should be concerned by. "Our understanding of bias is improving, and our priorities are set on the right targets," said Fanelli.

But that's no cause for complacency, he said. "We perhaps understand bias better, but we are far from having rid science of it. Indeed, our results suggest that the challenge might be greater than many think because interventions might need to be tailored to the needs and problems of individual disciplines of fields. One-size-fits all solutions are unlikely to work."

## Solutions and interventions

Ioannidis likewise cautioned that the data are purely observational, not experimental, and the question of how to reduce bias is far from clear. For example, he said, just because small studies tend to give exaggerated results doesn't mean we should stop doing them. "One might say immediately, well, we need to do large studies," he said. "That would be an intervention. But you can't necessarily translate an association directly into an effective intervention."

"I think that one can take each one of these biases and say, 'Well, let's try to reduce it or eliminate it,'" he added. "Some of them are easier to reduce or eliminate, but then we have to see what that does to the wider scientific literature."

That said, Ioannidis said he believes that many fields would benefit from having both larger studies and the involvement of numerous authors who are close enough to monitor one another's work. "But that's something that is an extrapolation," he said.

Making science better is quite possible, he said. "Physics, for example, at some point decided that they've had enough of these tiny studies done by small teams, and they went for a multi-team collaborative model," he said. "That changed the entire paradigm of how they do research. It probably largely removed the problem of small-study bias."

When physicists work together on huge projects, said Ioannidis, "you don't have the problem of these thousands and tens of thousands of physicists, each one of them running their tiny experiment, and then just waiting to collate the results after the fact and trying to make sense of them."

Since each field of science has a slightly different profile of biases, it makes sense, he said, for each one to choose the best ways to reduce the biases afflicting their field.

"This has to be a grass-roots movement," Ioannidis said. "It has to be something that scientists believe is good for their science to do. Top-down approaches, such as institutions and funding agencies trying to promote best practices, could also help, but it has to be an agreement, and an agreement among all these stakeholders. And obviously, scientists need to believe that this is something that will help the results and their science to be more reliable."

A researcher at Leiden University also co-authored the paper. This research was entirely supported by the U.S. Office of Research Integrity.

Stanford's departments of Medicine and of Health and Research Policy also supported the work. **ISM**

# Researchers create three-dimensional bladder reconstruction

**By Jackie Flynn**

The way doctors examine the bladder for tumors or stones is like exploring the contours of a cave with a flashlight. Using cameras attached to long, flexible instruments called endoscopes, they find that it's sometimes difficult to orient the location of masses within the bladder's blood-vessel-lined walls.

This could change with a new computer-vision technique developed by Stanford researchers that creates three-dimensional bladder reconstructions out of the endoscope's otherwise fleeting images. With this fusion of medicine and engineering, doctors could develop organ maps, better prepare for operations and detect early cancer recurrences.

"The beauty of this project is that we can take data that doctors are already collecting," said Audrey Bowden, PhD, assistant professor of electrical engineering. A paper describing the work was published online March 8 in *Biomedical Optics Express*. Bowden shares senior authorship with Joseph Liao, MD, an associate professor of urology. The lead author is Kristen Lurie, PhD, a former postdoctoral scholar at Stanford who is now a software engineer at Google

Bladder cancer has among the highest recurrence rates of any cancer. Fifty to 70 percent of tumors return after removal, according to Liao. Being able to see each patient's bladder as a digital 3-D model could improve surgical planning and help doctors monitor cancer recurrence.

"Endoscopy of the bladder, called cystoscopy, is an integral part of cancer management. Anything you can do to improve endoscopy is helpful," Liao said. "Surgeons are always looking for better ways to see cancer in order to remove it more effectively."

## Broadly applicable technique

One of the technique's advantages is that doctors don't have to buy new hardware or modify their techniques significantly. Through **See BLADDER, page 3**

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STANFORD MEDICINE

# Antibody fights pediatric brain tumors in preclinical testing

**By Erin Digitale**

Five types of pediatric brain cancer were safely and effectively treated in mice by an antibody that causes immune cells to engulf and eat tumors without hurting healthy brain cells, according to a new study by researchers at the School of Medicine.

The immune therapy studied consists of antibodies against a cellular "don't eat me" signal called CD47. Developed at Stanford, the anti-CD47 antibodies are already being tested in early clinical trials in adults who have tumors outside the central nervous system. But they have never been tried against pediatric brain tumors until now.

Samuel Cheshier

The new study pitted anti-CD47 antibodies against human cancer cells that had been grown in a dish and implanted in mice. The tests targeted five aggressive pediatric brain tumors: Group 3 medulloblastoma, atypical teratoid rhabdoid tumor, primitive neuroectodermal tumor, pediatric glioblastoma and diffuse intrinsic pontine glioma.

"For many of these tumors, there's just no treatment," said Samuel Cheshier, MD, PhD, assistant professor of neurosurgery. "Diagnosis is synonymous with a death sentence."

The study was published March 15 in *Science Translational Medicine*. Cheshier shares senior authorship of the paper with Irving Weissman, MD, the Virginia and D.K. Ludwig Professor for Clinical Investigation in Cancer Research and professor of pathology and of developmental biology. The lead authors are postdoctoral scholar Sharareh Gholamin, MD, and senior research scientist Siddhartha Mitra, PhD.

### 'Very, very active tumor-killing'

Many childhood brain tumors are inoperable. Some also lack effective chemotherapy drugs, or require radiation and chemotherapy so toxic to the developing brain that they cause devastating long-term side effects. In contrast with the toxic profile of existing treatments, the preclinical trials conducted by Cheshier's team indicate that anti-CD47 antibodies specifically target cancer cells while leaving healthy brain cells alone.

"The most exciting aspect of our findings is that no matter what kind of brain tumor we tested it against, this treatment worked really well in the animal models," said Cheshier, who is also a pediatric neurosurgeon at Lucile Packard Children's Hospital Stanford. In mice that had been implanted with both normal human brain cells and human brain cancer cells, "there was no toxicity to normal human cells but very, very active tumor-killing in vivo," he said.

Given the encouraging results of the new study and the ongoing research on anti-CD47 antibodies in adults, the antibodies are expected to reach clinical trials in children with brain cancer in one to two years, he added.

The anti-CD47 antibodies help the immune system to detect an important difference between cancerous and healthy cells: Cancer cells make "eat me" signals that are displayed on their cell surfaces, while healthy cells do not. However, cancer cells hide these "eat me" signals by producing large quantities of CD47, a "don't eat me" protein that is found on the surface of both healthy and malignant cells. When CD47 is blocked by antibodies, immune cells called macrophages can detect the cancer cells' "eat me" signals. Macrophages then selectively target, engulf and destroy the cancer cells without harming healthy cells, because normal cells lack the "eat me" signals.

### Study highlights

The Stanford team conducted a long series of experiments using different combinations of tumor cells and healthy cells in culture, as well as in various mouse models in which human brain cancer cells had been implanted in mice. Highlights of their experiments included the following:

- The team confirmed that all the various cancers tested express the CD47 "don't eat me" signal, as well as an "eat me" signal called CRT.
- In a dish, Group 3 medulloblastoma cells treated with anti-CD47 antibodies were engulfed and eaten by macrophages, while healthy brain cells were not harmed.
- In mice with a partially functioning immune system that had been transplanted with any of the five types of pediatric brain tumors, treating the mice with anti-CD47 antibodies significantly reduced the presence of those tumors.
- In mice, the antibody crossed the blood-brain barrier in significant amounts after being injected into the peritoneal space. This was an important finding because some other forms of immunotherapy are unable to cross this barrier. In mice transplanted with Group 3 medulloblastoma, anti-CD47 antibodies were more effective at treating the primary tumor if given in the peritoneal space, but better at treating metastases if given directly into the cerebrospinal fluid.
- Mixing healthy human neural progenitor cells with anti-CD47 antibodies did not cause any damage to the neural progenitor cells, either in their viability or ability to proliferate, suggesting that the antibodies would not interfere with brain development.
- In mice with a fully functioning immune system that had been implanted with cells from a high-grade glioma cell line, anti-CD47 antibodies significantly prolonged survival of the animals, from an average of 21 days for those in the untreated group to 32 and 38 days for those receiving low and high doses of antibodies, respectively.
- In mice treated with anti-CD47 antibodies, their brains, examined after treatment, showed that macrophages concentrated at the sites of the tumors. Further tests showed that macrophages got inside the tumors.

The anti-CD47 antibodies did not completely eliminate all tumors, suggesting that the antibodies may not be able to completely penetrate large tumors, the researchers noted.

To maximize their effects, the antibodies will likely need to be combined with other forms of cancer treatment, a concept the researchers plan to investigate further, Cheshier said. In the future, patients may receive combinations of immune therapies and lower doses of standard cancer treatments, he said, adding, "The question is: Can we wisely combine immune therapies and other approaches to make cancer treatment more efficacious and less toxic?"

Anti-CD47 antibodies also may have an advantage over other immunotherapies in that they activate macrophages, which completely engulf and eat cancer cells, Cheshier noted. "In many forms of immunotherapy, the cells you target die and spill their contents, which can cause dysregulated immune responses," he said. Anti-CD47 antibodies may produce fewer such side effects, though the idea remains to be tested.

Other Stanford co-authors of the paper are medical students Abdullah Feroze, Rogelio Esparza and Michael Zhang; postdoctoral scholars Suzana Kahn, PhD, Anne Volkmer, MD and Stephen Willingham, PhD; research assistants Anitha Ponnuswami, Theresa Storm, Cyndhavi Narayanan and Pauline Chu; senior research associate Jie Liu, MD, PhD; undergraduate research associate Chase Richard; Aaron McCarthy, a former life sciences research professional and animal colony manager; Patricia Lovelace, research and development engineer; Simone Schubert, life science researcher; visiting scholar Gregor Hutter, MD, PhD; Griffith Harsh, MD, professor of neurosurgery; Michelle Monje, MD, PhD, assistant professor of neurology; Yoon-Jae Cho, MD, a former assistant professor of neurology and neurological sciences; Ravi Majeti, MD, PhD, associate professor of medicine; senior scientist Jens Volkmer, MD; Paul Fisher, MD, professor of pediatrics; Gerald Grant, MD, associate professor of neurosurgery; Gary Steinberg, MD, PhD, professor of neurosurgery; Hannes Vogel, MD, professor of pathology and of pediatrics; and Michael Edwards, MD, professor of neurosurgery.

Cheshier, Monje, Majeti, Fisher, Grant and Edwards are members of Stanford's Child Health Research Institute. Cheshier, Weissman, Harsh, Monje, Majeti, Fisher, Grant, Vogel and Edwards are members of the Stanford Cancer Institute.

Scientists from SickKids, the Hospital for Sick Children in Toronto; University Hospital, Dusseldorf; and Johns Hopkins University also contributed to the study.

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Stanford's Department of Neurology & Neurological Sciences also supported the work. **ISM**

# Bladder

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the use of advanced computer-vision algorithms, the team reconstructed the shape and internal appearance of a bladder using the video footage from a routine cystoscopy, which would ordinarily have been discarded or not recorded in the first place.

"In endoscopy, we generate a lot of data, but currently they're just tossed away," said Liao.

Although the team developed the technique for the bladder, it could be applied to other hollow organs where doctors routinely perform endoscopy, including the stomach or colon. "We were the first group to achieve complete 3-D bladder models using standard clinical equipment, which makes this research ripe for rapid translation to clinical practice," Lurie said.

According to Liao, these three-dimensional images could help doctors prepare for surgery. Lesions, tumors and scars in the bladder are hard to find, both initially and during surgery.

"Sometimes you don't have a sense — where was I in the bladder?" Liao said. Seeing a three-dimensional rendering of an organ before operating, like having a map before embarking on a trip, could make the procedure easier for doctors. Other potential applications include using the digital 3-D reconstruction as a visual medical record.

### Accurate rendering

To test the accuracy of their bladder reconstruction, the team first created a model based on endoscopy images taken in a three-dimensional-printed bladder, known as a tissue phantom. Because the details of the tissue phantom are known, the researchers could directly compare it to their rendering. According to Bowden, tissue phantoms provide a standard for biological modeling analysis. The team found that its three-dimensional rendering matched the tissue phantom with few errors.

Audrey Bowden

Joseph Liao

This technique is the first of its kind and still has room for improvement, the researchers said. Primarily, the 3-D models tend to flatten out bumps on the bladder wall, including tumors. With the model alone, this may make tumors harder to spot. The team is now working to advance the realism, in shape and detail, of the models.

Future directions, according to the researchers, include using the algorithm for disease and cancer monitoring within the bladder over time to detect subtle changes, as well as combining it with other imaging technologies.

"The technology has immense potential, not to mention the fun factor to be able to navigate around a virtual organ," Liao said.

The other Stanford co-author of the paper is Dimitar Zlatev, MD, a resident in urology. A researcher at Max Planck Institute in Germany was also a co-author.

Bowden is a member of Stanford Bio-X and of the Stanford Child Health Research Institute. Liao is a member of Stanford Bio-X and of the Stanford Cancer Institute.

This research was supported by the National Science Foundation and the Max Planck Center for Visual Computing and Communication.

Stanford's departments of Urology and of Electrical Engineering also supported the work. **ISM**

# After years of preparation, students 'match' to residencies

**By Tracie White**

At 8:55 a.m., as Nuriel Moghavem got up from his table to accept the sealed, red envelope with his future hidden inside, his two younger brothers punched him in the shoulder — for luck.

The neurologist-in-training, who is also passionate about health care policy and took a year off from medical school to work as a legislative assistant in Sacramento, was, for the moment, at loose ends.

"Oh yeah, now I'm nervous," said Moghavem, taking deep breaths and staring at his shoes while his brothers grinned at him from behind.

He was one of 70 soon-to-be graduating Stanford medical students who took part in Match Day on March 17 at the Li Ka Shing Center for Learning and Knowledge. Thousands of other medical students across the United States were, at the same moment, also waiting to find out where they would be spending the next three or more years of their lives as residents. The scene was nerve-wracking.

"You kind of put all your eggs in one basket, and today you're going to see if they hatch," said Kelsey Hirotsu, who dressed up in heels and curls to find out where she would be matching in dermatology. Her parents' flight from Ohio was delayed due to bad weather, and her mom was "freaking out," Hirotsu said, laughing as she repeated her mom's frenzied cry, "We're not going to be there for the envelopes!"

### 'Congratulations to all of you'

Lloyd Minor, MD, dean of the School of Medicine, opened the ceremonies, applauding the accomplishments of the students, and congratulating them: "You're embarking upon a tremendously exciting period in your career and your life of medicine," he said. "Congratulations to all of you."

Next, Charles Prober, MD, senior associate dean for medical education, took the podium to start the countdown.

"The envelopes cannot be opened, anywhere in the country, until 9 a.m. Pacific time," Prober told the crowd of students, families, friends and advisers seated at tables in Berg Hall. With several minutes left to wait, Prober described for the crowd some of the history of Match Day.

The matching process is a tradition that dates back to 1952, with residency assignments ultimately determined by a nonprofit organization, the National Resident Matching Program. The organization uses a computer algorithm to align the choices of the applicants with those of the residency programs. It's a roughly yearlong process for medical students who, in their final year of medical school, fill out applications in the summer, then travel across the country to interviews in the fall. This year's students logged maybe a million frequent flier miles, traveling to a thousand or so interviews, Prober said.

Then with just one minute left before the big moment, Prober gave the crowd a few clues as to what was waiting inside the soon-to-be opened envelopes. The 70 students would be matching into 20 different disciplines. About 47 percent were matching into general disciplines, such as family medicine and pediatrics, while the remaining 53 percent were matching into sub-specialties, such as neurology, plastic surgery and ophthalmology.

"Sixty-six percent are going to two states: California and Harvard," Prober said — Harvard traditionally is a popular matching spot for Stanford students — to laughter from the crowd. "Twenty-nine percent are staying at Stanford."

### 'Ten, nine, eight …'

Finally, Prober started counting down the seconds: "Ten, nine, eight …." At exactly 9 a.m., the students began ripping open their envelopes, and the screams erupted, followed by hugs, tears and dozens of photos.

"I'm so happy, so happy!" yelled Hirotsu, who matched in dermatology, hugging her classmate and friend Monica Coughlan, both in tears. "I'm going to Stanford." Hirotsu's boyfriend grinned and said how hard she had worked to get to this day, adding that her parents should be arriving any moment.

Coughlan matched in orthopedic surgery at the University of California-San Francisco.

"I'm so incredibly happy," said Coughlan, adding that while opening her letter, "I literally almost collapsed."

Across the room, Moghavem took his time.

He watched as emotion erupted around the room, then with his parents and brothers gathered close around, he carefully opened his envelope with shaking hands, read the letter, nodded his head and hugged his mom. He matched at Stanford, his first choice.

"We have big shoes to fill," said his brother, Eli Moghavem, nodding to the youngest brother, a senior in high school, who was busy uploading the news to his friends on Snapchat.

His mom beamed with pride at her oldest son, the one who said in kindergarten that he wanted to be a pathologist, who was always kind and caring and "always has to do the right thing."

Moghevam said that making a difference in people's lives is what motivates him. American-born but of Iranian descent, he worried about other Iranian-born medical students matching this day whose plans may have been disrupted by the Trump administration's proposed travel ban.

"I'm fortunate. I was born in this country so I didn't have to worry about that, although my family all comes from Iran," he said, adding that he's the first doctor in his large, extended family.

"I expect a lifetime of family members sending me weird pictures of their rashes," he said. His shoulders sagged a bit with relief and joy, and he smiled. ISM

PHOTOS BY JOHN GREEN

Graduating medical students Grace Laidlaw, Tom Roberts and Grace Hunter compare results on Match Day after they and their peers were handed envelopes revealing where they would be spending their residencies.


(Clockwise from top left) Nuriel Moghavem learned that he was accepted to the residency program in neurology at Stanford. Monica Coughlan, left, and Arhana Chattopadhyay talk during Match Day at the Li Ka Shing Center for Learning and Knowledge. Coughlan matched to UCSF in orthopedic surgery, and Chattopadhyay matched to plastic surgery at Stanford. Mark Gaertner poses for a photo with his girlfriend, Lyly Truong, after learning he was accepted to the residency program in neurology at UCLA.

# Researchers look to Lego for automation of biology experiments

**By Andrew Myers**

Elementary and secondary school students who later want to become scientists and engineers often get hands-on inspiration by using off-the-shelf kits to build and program robots. But so far it's been difficult to create robotic projects to foster interest in the "wet" sciences — biology, chemistry and medicine — so called because experiments in these fields often involve fluids.

Now, Stanford bioengineers and their collaborators have shown how an off-the-shelf kit can be modified to create robotic systems capable of transferring precise amounts of fluids between flasks, test tubes and experimental dishes.

By combining the Lego Mindstorms robotics kit with a cheap and easy-to-find plastic syringe, the researchers created a set of liquid-handling robots that approach the performance of the far more costly automation systems found at universities and biotech labs.

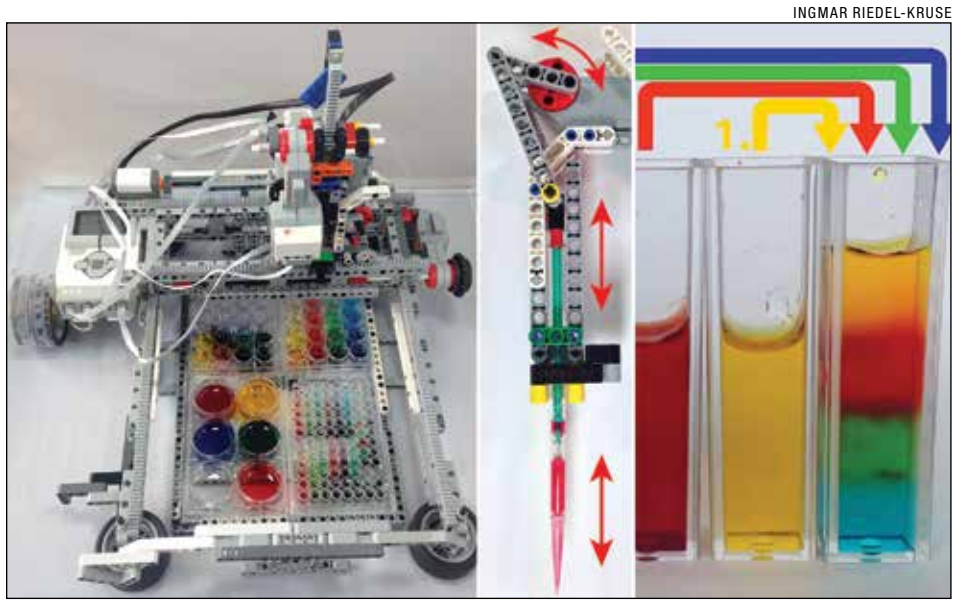
"We really want kids to learn by doing," said Ingmar Riedel-Kruse, PhD, assistant professor of bioengineering.

"We show that with a few relatively inexpensive parts, a little training and some imagination, students can create their own liquid-handling robots and then run experiments on them — so the students learn about engineering, coding and the wet sciences at the same time," he added.

### Robots meet biology

A paper describing the work was published March 21 in *PLoS Biology*. Riedel-Kruse is the senior author. The lead author is postdoctoral scholar Lukas Gerber.

INGMAR RIEDEL-KRUSE




**Building a liquid-handling robot: Start with a Lego Mindstorms system (left); add a motorized pipette for dropping fluids (center); and then perform simple experiments, such as showing how liquids of different salt densities can be layered.**

The robots are designed to pipette fluids from and into cuvettes and multiple-well plates — types of plastic containers commonly used in laboratories. Depending on the specific design, the robots can handle liquid volumes far smaller than 1 microliter, a droplet about the size of a single coarse grain of salt. Riedel-Kruse believes that these Lego designs might even be useful for specific professional or academic liquid-handling tasks that normally require robots costing many thousands of dollars.

His overarching idea is to enable students to learn the basics of robotics and the wet sciences in an integrated way. Students could learn to collaborate while also developing STEM skills, such as mechanical engineering and computer programming. They could also gain a deeper appreciation of the value of robots in life sciences experiments.

Riedel-Kruse said he drew inspiration from constructionism, a learning theory that advocates project-based learning in which students make tangible objects and connect different ideas and areas of knowledge and thereby construct mental models to understand the world around them. One of the leading theorists in the field was Seymour Papert, whose seminal 1980 book Mindstorms was the inspiration for the Lego Mindstorms sets.

**"We really want kids to learn by doing."**

"I saw how students and teachers were already using Lego robotics in and outside school, usually to build and program moving car-type robots, and I was excited by that," he said. "But I saw a vacuum for bioengineers like me. I wanted to bring this kind of constructionist, hands-on learning with robots to the life sciences."

### Do it yourself

In their *PLoS Biology* paper, the team members offer step-by-step building plans and several fundamental experiments targeted to elementary, middle and high school students. They also offer experiments that students can conduct using common household consumables like food coloring, yeast or sugar. In one experiment, colored liquids with distinct salt concentrations are layered atop one another to teach about liquid density. Other tests measure whether liquids are acids, like vinegar, or bases, like baking soda, or which sugar concentration is best for yeast. Yet another experiment uses color-sensing light meters to align color-coded cuvettes.

The coding aspect of the robot is elementary, Riedel-Kruse said. A simple programming language allows students to place symbols telling the robot what to do: Start. Turn motor on. Do a loop. And so forth. The robots can be programmed and operated in different ways. In some experiments, students push but-

**See LEGO, page 8**

# As Moore's law hits limits, new generation of brainlike computers emerges

**By Nathan Collins**

For five decades, Moore's law held up pretty well: Roughly every two years, the number of transistors that could fit on a chip doubled, all while costs steadily declined. Today, however, transistors and other electronic components are so small they're beginning to bump up against fundamental physical size limits.

Moore's law has reached its end, and it's going to take something different to meet the need for computing that is ever faster, cheaper and more efficient.

As it happens, Kwabena Boahen, PhD, a Stanford professor of bioengineering and of electrical engineering, has a pretty good idea what that something more is: brainlike, or neuromorphic, computers that are vastly more efficient than the conventional digital computers we've grown accustomed to.

This is not a vision of the future, Boahen said. As he lays out in the March/April issue of *Computing in Science and Engineering*, the future is now.

"We've gotten to the point where we need to do something different," said Boahen, who is also a member of Stanford Bio-X and the Stanford Neurosciences Institute. "Our lab's three decades of experience has put us in a position where we can do something different, something competitive."

### 30 years in the making

It's a moment Boahen has been working toward his entire adult life, and then some. He first got interested in computers as a teenager growing up in Ghana. But the more he learned, the more traditional computers looked like a giant, inelegant mess of memory chips and processors connected by weirdly complicated wiring.

Both the need for something new and the first ideas for what that would look like crystalized in the mid-1980s. Even then, Boahen said, some researchers could see the end of Moore's law on the horizon. As transistors continued to shrink, they would bump up against fundamental physical limits on their size. Eventually, they'd get so small that only a single lane of electron traffic could get through under the best circumstances. What had once been electron superfreeways would soon be tiny mountain roads, and while that meant engineers could fit more components on a chip, those chips would become more and more unreliable.

At around the same time, Boahen and others came to understand that the brain had enormous computing power — orders of magnitude more than what people have built, even today — even though it used vastly less energy and remarkably unreliable components: neurons.

### How does the brain do it?

While others have built brain-inspired computers, Boahen said, he and his collaborators have developed a five-point prospectus — manifesto might be the better word — for how to build neuromorphic computers that directly mimic in silicon what the brain does in flesh and blood.

The first two points of the prospectus concern neurons themselves, which unlike computers operate in a mix of digital and analog mode. In their digital mode, neurons send discrete, all-or-nothing signals in the form of electrical spikes, akin to the ones and zeros of digital computers. But they process incoming signals by adding them all up and firing only once a threshold is reached — more akin to a dial than a switch.

That observation led Boahen to try using transistors in a mixed digital-analog mode. Doing so, it turns out, makes chips both more energy efficient and more robust when the components do fail, as about 4 percent of the smallest transistors are expected to do.

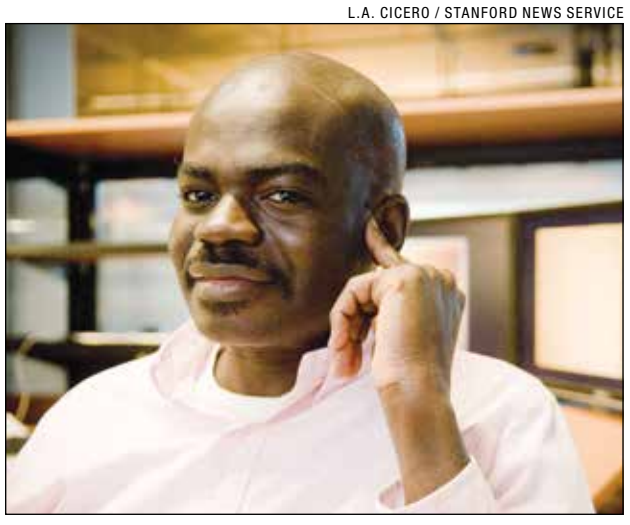
From there, Boahen builds on neurons' hierarchical organization, distributed computation and feedback loops to create a vision of an even more energy efficient, powerful and robust neuromorphic computer.

### The future of the future

But it's not just a vision. Over the last 30 years, Boahen's lab has actually implemented most of its ideas in physical devices, including Neurogrid, one of the first truly neuromorphic computers. In another two or three years, Boahen said, he expects they will have designed and built computers implementing all of the prospectus's five points.

Don't expect those computers to show up in your laptop anytime soon, however. Indeed, that's not really the point: most personal computers operate nowhere near the limits on conventional chips. Neuromorphic computers would be most useful in embedded systems that have extremely tight energy requirements, such as very low-power neural implants or on-board computers in autonomous drones.

L.A. CICERO / STANFORD NEWS SERVICE



**Kwabena Boahen has written "A Neuromorph's Prospectus," outlining how to build computers that directly mimic in silicon what the brain does in flesh and blood.**

"It's complementary," Boahen said. "It's not going to replace current computers."

The other challenge: getting others, especially chip manufacturers, on board. Boahen is not the only one thinking about what to do about the end of Moore's law or looking to the brain for ideas. IBM's TrueNorth, for example, takes cues from neural networks to produce a radically more efficient computer architecture. On the other hand, it remains fully digital, and, Boahen said, 20 times less efficient than Neurogrid would be had it been built with TrueNorth's 28-nanometer transistors.

Boahen is also a member of Stanford SystemX and the Stanford Computer Forum. His work was supported by a Director's Pioneer Award and a Transformative Research Award from the National Institutes of Health and a grant from the U.S. Office of Naval Research. **ISM**

## Blinded

**continued from page 1**

cells some researchers are targeting to develop therapies.

"There is a lot of very well-founded evidence for the positive potential of stem therapy for many human diseases, but there's no excuse for not designing a trial properly and basing it on preclinical research," Goldberg said.

The "trial" lacked nearly all of the components of a properly designed clinical trial, including a hypothesis based on laboratory experiments, assignment of a control group and treatment group, collection of data, masking of clinical and patient groups, and plans for follow-up, Goldberg and Albini said. "There was a whole list of egregious things," Albini said.

Listings on ClinicalTrials.gov are not fully scrutinized for scientific soundness, Goldberg said. Although still visible on the website, the listing now states: "This study has been withdrawn prior to enrollment." The clinic is also no longer performing these eye injections, although it is still seeing patients, Albini said.

### 'It's alarming'

The procedures were arguably not subject to Food and Drug Administration approval because the cells were not transferred between patients and were considered "minimally processed," according to Title 21, Part 1271.10, of the Code of Federal Regulations. The FDA released more specific guidelines in October 2015, after these procedures were performed, establishing the requirement for FDA oversight and approval for these types of procedures.

"We expect health care providers to take every precaution to ensure patient safety, but this definitely shows that the lack of oversight can lead to bad players and bad outcomes. It's alarming," Albini said.

The authors acknowledged that it is difficult for patients to know whether a clinical trial, or a stem cell therapy, is legitimate. Goldberg recommended that patients considering a stem cell treatment consult a website, A Closer Look at Stem Cells, maintained by the International Society for Stem Cell Research. It is also advisable to check if a trial is affiliated with an academic medical center, Goldberg said.

> "There's no excuse for not designing a trial properly and basing it on preclinical research."

The lead author is Ajay Kuriyan, MD, assistant professor of ophthalmology at the University of Rochester Medical Center. Researchers from the University of Miami, University of Rochester, University of Oklahoma and the Center for Sight also co-authored the study.

The report was funded by the National Institutes of Health, Research to Prevent Blindness, the Department of Defense and the Klorfine Foundation.

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

## Gun

**continued from page 1**

**Thomas Weiser**

**Sarabeth Spitzer**

little research on gun violence from a public health perspective. This is, in part, due to a measure Congress passed in 1996 that restricts federal funding for firearms research, Spitzer said.

Past studies have looked into the total costs of firearm injuries — medical as well as social — but most have focused either on particular states or within narrow time ranges. Analyzing data from 2012, a *Mother Jones* investigation estimated that the annual cost of gun violence in America exceeds $229 billion, as much as $3.4 billion of which includes emergency services, police investigations and long-term medical- and mental-health care costs. The actual costs of hospital visits are difficult to tease out from these figures, and it is unclear who actually ends up paying for them.

"Firearm injuries are tied to one of the most controversial political issues in the country, so it is important for all sides to have access to fact-based research," Spitzer said. "Cost information can be especially helpful when making health policy decisions."

The Stanford team set out to estimate the national medical costs of firearm injuries over a nine-year period by using publicly available data in the Nationwide Inpatient Sample, the largest database in the United States, which houses information from about 8 million hospital discharges each year. The researchers picked patients who were admitted for firearm-related injuries and analyzed the severity of their wounds, the cost of their care, where they were hospitalized and how they paid for the hospitalizations.

### Government bears large share of cost

Spitzer and her colleagues interrogated the data to address two primary questions: What were the total medical costs when gunshot victims were first hospitalized, and where did the financial burden of medical care fall?

The team found that the government bears about 40 percent of the total costs. "It's a very high financial burden," Spitzer said.

The researchers found that victims paid for hospital costs through Medicare, Medicaid, private insurance or out of their pockets. Patients were overwhelmingly male, and there was a correlation between their insurance status and how they sustained their injuries. For example, shootings of young and poor individuals insured by Medicaid comprised two-thirds of firearm injuries, and they were most often victims of assault. In contrast, older Medicare-insured patients were more likely to suffer from self-inflicted gunshot wounds.

The study captures costs for a very limited experience because the costs of firearm injuries continue in many different ways, Spitzer said. "There's a cost if you're readmitted, there's long-term rehab, and a lot of these patients end up needing long-term health care," she said, adding that she and her colleagues will next systematically analyze costs of hospital readmissions.

"It's amazing that we don't know as much about the medical costs of firearm injuries," said David Hemenway, director of the Harvard Injury Control Center, who was not involved in the study. "[This study] highlights that this is just the tip of the iceberg."

Other Stanford co-authors of the study are Kristan Staudenmayer, MD, associate professor of surgery; David Spain, MD, professor of surgery; and research scientist Lakshika Tennakoon.

The research was supported by the Stanford Medical Scholars Fellowship Program. **ISM**

# Fathers, in addition to mothers, now sought for Stanford eating-disorder study

**By Erin Digitale**

VGSTOCKSTUDIO / SHUTTERSTOCK.COM

Mothers who have previously had an eating disorder often struggle to teach their children healthy eating habits, research has shown. Now, a School of Medicine study of how to help them is being expanded to include fathers, making it the first study in the world to offer this type of targeted intervention for dads.

"We have really sparse information on fathers with eating disorders," said Shiri Sadeh-Sharvit, PhD, a visiting scholar at Stanford who is helping to lead the new study. "Although eating disorders are very stigmatized in women, there is even more stigma in men. And men may not understand the potential impact of their eating disorder on their children, since feeding is, in many families, still perceived as an issue that mothers worry more about."

In 2014, Sharvit and her collaborators began testing a method aimed at helping mothers with a history of eating disorders nurture good eating habits in their young children. The researchers began their study in women who were living with their partners and small children. The eligibility criteria for the study have been extended, and the researchers are now recruiting families with a child between the ages of 1 and 5 whose mother or father has had anorexia nervosa, bulimia nervosa or binge-eating disorder in the past. The study had previously included only two-parent families; single-parent families are now also being asked to join. For the 16-week study period, the researchers will work with the parent to build healthy family interactions around food.

### Unhealthy control

Prior research has shown that parents with a history of disordered eating may try to exercise an unhealthy degree of control over their children's food intake. For instance, parents who fear their children becoming overweight may prevent their kids from eating high-fat or high-carbohydrate foods that are needed for healthy development. Or, the parents may closely monitor how much a child eats and tell him or her when to stop eating.

Such well-intentioned efforts can backfire, Sharvit said. "There is a lot of evidence that the more you control or restrict a child's eating, the more likely they are to eat more when the parent is not around and become overweight."

In the newly expanded study, the Stanford researchers will meet with families 12 times during the 16-week period. Parents will learn about the "Division of Responsibility" model of feeding, in which parents are in charge of the timing and content of a meal, and children decide whether to eat and how much. The researchers will also help each family identify specific, individualized ways that the parent's eating-disorder history might affect them and develop techniques to counteract possible problems.

"We want to help educate parents and also help them work through their anxieties that if they open the gate, the child will have no limit," Sharvit said. "We want to help parents feel that they can manage their own concerns and allow their child to regulate his or her own hunger and satiety."

The researchers hypothesize that the study will help parents avoid pressuring children to eat too little or too much, that children will take more responsibility for regulating their own hunger and fullness, and that parents will communicate better about eating patterns.

The study's principal investigator is James Lock, MD, PhD, professor of psychiatry and behavioral sciences at Stanford and a clinician who treats eating disorders at Lucile Packard Children's Hospital Stanford.

Families who are interested in participating in the research can contact Sadeh-Sharvit at 497-4949 or shiris@stanford.edu for more information.

Information about all of Stanford's eating-disorder studies that are seeking participants is available online at http://edresearch.stanford.edu/studies.html. **ISM**

5 QUESTIONS

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

# Adelsheim on Santa Clara County suicide report

*Earlier this month, the federal government released a report on risk factors for suicide among youth in Santa Clara County. The report, which was requested by members of the Palo Alto community in response to youth suicides in 2009 and 2014, reviewed the epidemiology of suicidal behaviors in young people living in the county, as well as aspects of the community response. Steven Adelsheim, MD, clinical professor of psychiatry and behavioral sciences at the School of Medicine and a child and adolescent psychiatrist at Lucile Packard Children's Hospital Stanford, has been involved in several efforts to improve mental health care for young people in the community. He spoke with science writer Erin Digitale about the new report, which was produced by the Centers for Disease Control and the Substance Abuse and Mental Health Services Administration.*

### 1 What did the report say about suicide rates and precipitating circumstances behind youth suicides in Santa Clara County?

**ADELSHEIM:** The report found that youth suicide rates for residents of Santa Clara County have remained really stable, with no significant difference over time since 2003. When you look across the board at the county's 10- to 24-year-olds, the annual suicide rate is 5.4 per 100,000 people, which is very similar to the California rate of 5.3 per 100,000. The national suicide rate among this age group is higher than rates for our county and state, at about 8 per 100,000.

Looking at the county's youth suicides in detail, two-thirds occurred among young people aged 20 to 24, and three-fourths of young people who died by suicide were male. Their ethnicity distribution was close to that of the county as a whole. When the researchers looked at youth who died by suicide, the cities of Palo Alto and Morgan Hill did have higher rates than the county as a whole: 14.1 suicide deaths per 100,000 among Palo Alto residents and 12.7 per 100,000 among Morgan Hill residents.

A key finding of the report was that many people who died by suicide had faced a recent crisis or mental health issue. About a third were currently being treated for mental illness, and 48 percent had current mental health problems, including depression, substance abuse and alcohol dependence. Fifty-two percent had had a recent life crisis, such as a breakup with a boyfriend or girlfriend, problems at school or a significant argument.

Steven Adelsheim

### 2 To what extent do you think the findings support or refute assumptions people may have made about youth suicides in Santa Clara County?

**ADELSHEIM:** Locally, before the report came out, there was a sense that losses of young people in the Palo Alto area were much larger compared to the county as a whole. It's true that the rate of youth suicides within Palo Alto was found to be higher than for young people elsewhere in the county, and there may be some ongoing stressors among Palo Alto youth, such as academic stress, that the community is working hard to address. But the findings also make clear that no single factor explains suicide-related deaths.

The report reflects well on efforts the Palo Alto community has been making to improve all aspects of mental health among young people. Strong partnerships have been formed between the school district, the city, parents, teens, mental health care providers — including our team at Stanford — and many others. All these partners deserve credit because their efforts are making a difference.

### 3 What else did the report reveal?

**ADELSHEIM:** When you look broadly at the entire county and note the rate of suicides in males aged 20 to 24, it raises important questions about how young people who are no longer high school age can access mental health services. I think we need to recognize their crises and build better access to early mental health care across the board. We also need to start asking why these young men are less likely to access mental health care and build programs for them to easily get it.

The contrast between youth suicide rates in rural and urban areas of Northern California is also noteworthy. According to the data the CDC examined, Bay Area counties have rates that are very similar to the state rate of around 5 to 6 suicide deaths per 100,000 young people, while rural counties have much higher rates. The top three were Mendocino (16.2 per 100,000), Lake (15.2 per 100,000) and Humboldt (12.5 per 100,000) counties.

One difficulty is that many rural counties generally lack the financial support to provide the same access to evidence-based interventions across large rural areas. A possible solution is building out telehealth and telepsychiatry capacity, which we at Stanford have done in a small way by providing this kind of support to a pediatric practice in Monterey. There may be value in expanding these types of support to more rural counties to expand access to mental health care.

### 4 One area of focus for the CDC report was the quality of news reporting about Santa Clara County's youth suicides. What does the media need to improve?

**ADELSHEIM:** Responsible news reporting is an important element of reducing suicide contagion among youth, but the CDC report shows that local and national coverage of youth suicides was fairly uneven in quality. Problems the CDC documented in media reports included use of sensationalistic terms and headlines, as well as photos or language depicting the means by which people had died. Those should be avoided in news coverage of suicides.

Also, there are several things media stories can include to make coverage more responsible, which the report found were sometimes missing. For instance, it helps to talk about suicide as a public health issue that is multifactorial and can have important mental health aspects. It's useful to talk about hope and tell stories of people who were struggling but then did better. And it's very important to say that treatment for mental health problems works, to say there are treatment options, and to provide contact information for crisis services and say, "If you're concerned that you may harm yourself, here is the place to go." Overall, avoiding sensationalism and showing that help is available are really important.

### 5 How have Stanford Children's Health and Lucile Packard Children's Hospital Stanford responded to the need for better mental health services for our community's youth?

**ADELSHEIM:** We have formed many productive partnerships. We're doing a lot of work with schools in Santa Clara and San Mateo counties, where we've been providing direct care, prevention efforts, early intervention, and training and support for school staff around suicide prevention. We're working with groups like Project Safety Net in Palo Alto and the HEARD Alliance to increase the range of support available for young people, as well as providing community education. We're also working to launch a program for youth with early signs of psychosis to help decrease suicide risk among those in the early stages of serious psychiatric conditions.

In addition, we've partnered with Mills Peninsula Hospital to have Stanford child and adolescent psychiatrist staff several pediatric inpatient mental health beds. Having hospital beds available for youth in crisis is important, but only one piece of the puzzle. We also want to be able to help young people much earlier. To that end, we've been developing a local version of the headspace program, based on a successful Australian program of the same name, for providing outpatient counseling and other early-intervention services to youth. Santa Clara County has allocated funding for two staff positions, a youth development specialist and a school employment specialist, and we're partnering with the county to potentially access additional innovation grant funding to support the development of two county headspace sites.

The headspace model is designed to help youth aged 12 to 25, so it's a potential access point for young people aged 20 to 24 who might not otherwise get mental health care. Our marketing for headspace will include messages saying that this is a place to go for help recovering from breakups and other difficult life events, rather than overtly branding it as a mental health clinic. We hope this approach will help us draw in a larger swath of young people.

Overall, we are supporting a broad range of community-based services. We want to have capacity that stretches from prevention to early intervention to acute-care services, and we're really proud to partner with so many community groups to work toward this worthy goal.

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*Individuals in crisis can receive help from the Santa Clara County Suicide & Crisis Hotline at (855) 278-4204. Help is also available from anywhere in the United States via Crisis Text Line (text HOME to 741741) or the National Suicide Prevention Lifeline at (800) 273-8255. All three services are free, confidential and available 24 hours a day, seven days a week.* **ISM**

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# Drama

**continued from page 1**

they love. The people they want to punish are often those who are least likely to learn something, and those who are most likely to be hurt are not the ones they wanted to hurt in the first place."

In the Netflix series, Hannah's mother is a much more prominent character than in the novel, and the series shows her pain and sadness, Hu said.

Another problem with the book: The school counselor Hannah approaches for help comes across as inept.

"We didn't want teens to feel like if they went to adults for help, the adults would be uncaring," Hu said. The dialogue for Hannah's interaction with the counselor remained the same as in the novel, but at Hu's advice, the counselor was given a back story, and script writers added several nonverbal details to his conversation with Hannah. For instance, the phone rings repeatedly while they talk, and the counselor closes his eyes or shakes his head at difficult parts of the conversation, indicating to Hannah that he may be too busy to help her, or not willing to hear what she is saying.

"The producers did a nice job of depicting little things that add up to someone missing something important," Hu said. "I'd like to use the scene to help teach medical students and residents."

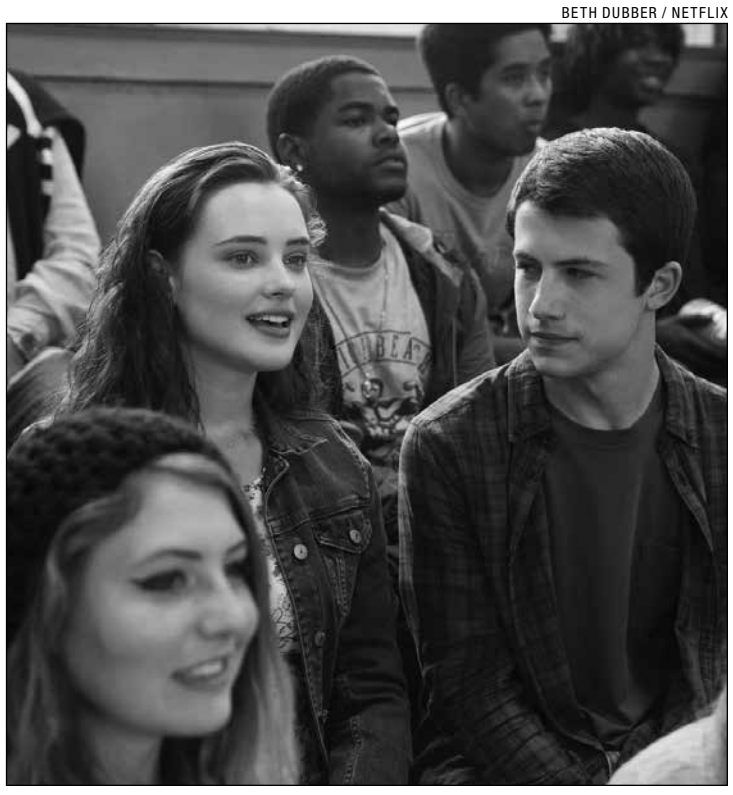
### Depicting the bullies

Hu also advised the producers on portraying the bullies, as well as the scene in which Hannah dies. "I wanted to make sure the bullies are depicted as people, and show that people can contribute to bullying in ways that are maybe thoughtless but not malicious," she said. If the bullies were too one-dimensional, it would be easy for viewers to dismiss them as simply mean; showing them as real people is more likely to prompt viewers to think through how they treat their own peers.

The scene in which Hannah dies, Hu said, "had to be sad, lonely and not inspire copycats." Instead of the Romeo-and-Juliet glamour used in many fictionalized depictions of suicide, the producers showed Hannah in a baggy sweatshirt, in pain, crying.

"We wanted to convey that suicide isn't a good option; instead it is the end of all options and inflicts pain on people you love," Hu said. "And we wanted to show that you can get help, that Hannah misses opportunities for help and that teens around her have opportunities to help her." **ISM**

BETH DUBBER / NETFLIX



***13 Reasons Why*, a drama about teen suicide, debuts March 31 on Netflix.**

# Conference on future of medical education set for April 22-23

**By Tracie White**

Stanford Medicine X|ED, an academic conference on the future of medical education, will be held April 22-23 at the Li Ka Shing Center for Learning and Knowledge at the School of Medicine.

In its inaugural year as a stand-alone conference, the event will focus on how to increase diversity within the health care workforce and among medical educators, and the application of "precision education" — meeting the needs of future learners through new technology and tools, and personalized education.

The Medicine X|ED conference began two years ago as a part of the academic health-innovation conference Medicine X, but it has been spun off as a separate event this year.

"Medicine X aims to transform health care by elevating under-heard voices from its front-line stakeholders, including patients, caregivers, providers — people with expertise to transform academic medicine from the bottom up," said Lawrence Chu, MD, professor of anesthesiology, perioperative and pain medicine at Stanford and founder and director of Medicine X. "We realized that in order to make real impactful change in health care, we needed to dedicate resources to reach the future leaders of tomorrow early enough to make a difference. Medicine X|ED is our answer to that unmet need."

COURTESY OF STANFORD MEDICINE X


Charles Prober, senior associate dean for medical education, speaks last year at Stanford Medicine X | ED, an event that focuses on the future of medical education.

### Examining ways to improve medical education

The conference will bring together a broad range of stakeholders in health care education — from patients, to providers, researchers, industry leaders, designers, technologists and medical educators. The goal is to examine new methods of improving medical education, organizers said.

"We challenge educators to examine medical education in the ways we look at medical treatment, where we use data and analytics to better understand the entire person in order to tailor the best therapy and treatments for an individual person — precision health," Chu said. "This new concept, precision education, applies a similar notion to framing an educational experience, looking at a learner's entire learning footprint — how many times a learner interacts with an online learning management system, opens an email or webpage, quiz question, app, flash card."

Keynote speakers at the conference will be:

• Clay Johnson, MD, the inaugural dean of the new Dell Medical School at the University of Texas-Austin.

• Dan Schwartz, PhD, dean of the Stanford Graduate School of Education and the author of a new book, *The ABC's of How We Learn*.

• Neha Sangwan, MD, developer of a program for health care workers' own care, a program she calls "self-care in health care."

• Erik Brodt, MD, a physician who works to improve Native American health and medical training, who will speak about using digital media storytelling to inspire American Indian youth.

Key events over the two-day event include:

• Diversity 2.0 — a main stage breakout panel session focused on advancing the conversation on diversity and inclusion within medical education.

• Patient-Centered Outcomes Research and Comparative Effectiveness Research — a main stage breakout session.

• A main stage panel on the role of games in medical education, moderated by Parvati Dev, PhD, former director of Stanford University Medical Media and Information Technology.

Among the many workshops and learning labs, scheduled topics include design thinking for future doctors, integrating the expanding health care system, developing leadership and self-empowerment and games as a solution for medical training.

For more information or to register for the conference, visit: https://medicinex.stanford.edu/ed. ISM

## Team led by Sanjay Basu wins third place in data analysis contest

A team led by Sanjay Basu, MD, PhD, assistant professor of medicine, has been awarded third place in contest designed to promote the sharing of clinical trial data.

Contestants used a data set to identify a new scientific or clinical finding. The data set was developed during the Systolic Blood Pressure Intervention Trial, known as SPRINT, which compared intensive management to standard management of blood pressure.

The Massachusetts Medical Society sponsored the contest, called the SPRINT Data Analysis Challenge, which was held to promote the sharing and reuse of clinical trial data.

Basu's team used the data to develop and validate a clinical decision score that identifies patients who are likely to experience benefits and unlikely to experience harms when undergoing intensive blood pressure treatment. The work could potentially reduce the chance of life-threatening side effects, such as kidney failure.

Sanjay Basu

A first-, second- and third-place winner were selected from 143 entries based on which entry provided the most clinically useful information. Judging was done by a panel of experts and crowd-voting by the public.

The three winners will present their findings at a meeting in April.

Basu's team included Joseph Rigdon, PhD, a Stanford engineering research associate, and researchers from the University of Michigan. ISM

## OF NOTE

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

**RENUMATHY DHANASEKARAN**, MD, instructor of medicine, has received one of three 2017 Junior Faculty Development Awards from the American College of Gastroenterology. The award, which provides $100,000 a year for three years, supports junior investigators working toward independent careers in clinical research in gastroenterology or hepatology. Dhanasekaran's project is "Plasma glycoproteomic biomarkers for invasive human hepatocellular carcinoma," and her mentor is Dean Felsher, MD, PhD, professor of medicine and of pathology.

**ALFREDO DUBRA**, PhD, was appointed associate professor of ophthalmology, effective Oct. 1, 2016. His focus is on using ophthalmologic imaging technologies to reveal ocular, vascular, neurodegenerative and systemic diseases.

**DAVID KINGSLEY**, PhD, professor of developmental biology, has received the 2017 Genetics Society of America Medal. The award honors outstanding contributions to the field of genetics in the past 15 years. Kingsley was recognized for his experimental work, beginning with different species of three-spine stickleback fish, which provided insights into how vertebrates evolve in natural environments. He has now expanded his inquiry into understanding human traits, including aspects of skin, skeletal and brain evolution.

**KARIM SALLAM**, MD, clinical instructor of medicine, has received the American College of Cardiology's William W. Parmley Young Author Achievement Award. The award recognizes two papers published in the *Journal of the American College of Cardiology* by authors early in their careers. Sallam's paper, published Nov. 8, 2016, was "Patient-specific and genome-edited induced pluripotent stem cell-derived cardiomyocytes elucidate single-cell phenotype of Brugada syndrome." His mentor is Joseph Wu, MD, PhD, professor of medicine and of radiology and director of the Stanford Cardiovascular Institute. ISM

Renumathy Dhanasekaran

Alfredo Dubra

David Kingsley

Karim Sallam

## Lego

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tons to actuate individual motors. In other experiments, students preprogram all motor actions to watch their experiments executed automatically.

"It's kind of easy. Just define a few parameters, and the system works," he said, adding, "These robots can support a range of educational experiments, and they provide a bridge between mechanical engineering, programming, life sciences and chemistry. They would be great as part of in-school and after-school STEM programs."

### STEM-ready

Riedel-Kruse said these activities meet several important goals for promoting multidisciplinary STEM learning as outlined by the Next Generation Science Standards and other national initiatives. He stressed the cross-disciplinary instruction value that integrates robotics, biology, chemistry, programming and hands-on learning in a single project.

The team has co-developed these activities with students and a science teacher, and then tested them with elementary and middle school students over the course of several weeks of instruction. Instructions for developing the robots are now ready for wider dissemination to an open-access community that can expand upon the plans, capabilities and experiments for this new breed of fluid-handling robots, and they might even be suitable to support certain research applications.

"We would love it if more students, do-it-yourself learners, STEM teachers and researchers would embrace this type of work, get excited and then develop additional open-source instructions and lesson plans for others to use," Riedel-Kruse said.

For more information, see the *PLoS Biology* paper and Riedel-Kruse's lab website.

Other co-authors of the paper are a science teacher at Isaac Newton Graham Middle School in Mountain View and one current and two former high school students.

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Stanford's Department of Bioengineering, which is jointly operated by the School of Medicine and the School of Engineering, also supported the work. ISM