INSIDE STANFORD MEDICINE

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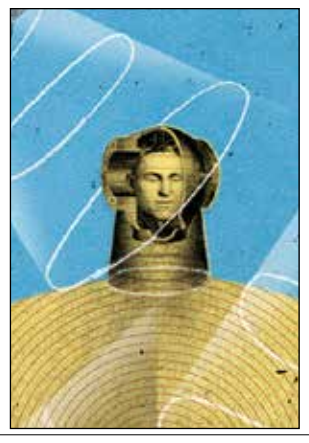

Scientists are harnessing noise and acoustics in technologies aimed at improving health.

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Introducing medicine to low-income teens

By Julie Greicius

STEVE FISCH

William Tate (left), a Stanford medical student, helped to teach an anatomy lab session July 6 to participants in the Stanford Medical Youth Science Program.

The categories were "muscles of the thorax," "health disparities," "lungs," "bones of the thorax" and "research and college prep."

Gathered in the living room of Roth House, on the Stanford University campus, on a recent Sunday evening, two-dozen high school juniors and seniors hit buzzers and threw their hands up in hopes of being chosen to answer. They were playing a quiz game that tested their knowledge from a week packed with medical lectures, labs, hospital internships and workshops on college admissions.

The game night capped week one of the Stanford Medical Youth Science Program, a free, five-week residential summer program for low-income high schoolers from Northern California who aspire to careers in the medical and health sciences. This summer's session is the program's 30th, and will bring its alumni roster to more than 700.

"This is an exciting year for us," said the program's executive director, Alivia Shorter.

The program was conceived by two Stanford pre-med students, Michael McCullough and Mark Lawrence, who in 1987 approached Marilyn Winkleby, MPH, PhD, now a professor emerita of medicine at the Stanford Prevention Research Center, seeking faculty sponsorship and financial support. Winkleby, who came from a low-income background herself, embraced the idea and helped sustain it for the next three decades. In 2011, the program was recognized with the U.S. Presidential Award for Excellence in Science, Mathematics and Engineering Mentoring.

"Dr. Winkleby saw that there are many talented, intellectually curious, passionate young people around, that if they just had a little more mentorship, we could change the trajectory of their careers and their lives," said Shorter, who also is director of diversity and outreach for Stanford Pre-Collegiate Studies, a set of programs for teens that includes the Stanford Medicine Youth Science Program.

'Hungry for education'

Winkleby said that in the program's first year, she helped recruit seven students from schools in East Palo Alto. "We've always focused on selecting students with a high potential but who are often overlooked," she said. "They're hungry for education, resources and knowledge."

The program combines science education, hands-on clinical experience and personal development. Strong bonds that form between the 10 Stanford undergraduate counselors and 24 high school participants — and among the participants themselves — create a sense of belonging and connection, according to several participants See PROGRAM, page 6

Medical errors may stem more from burnout than unsafe health care settings, study finds

By Tracie White

Physician burnout is at least equally responsible for medical errors as unsafe medical workplace conditions, if not more so, according to a study led by researchers at the School of Medicine.

"If we are trying to maximize the safety and quality of medical care, we must address the factors in the work environment that lead to burnout among our health care providers," said Tait Shanafelt, MD, director of the Stanford WellMD Center and associate dean of the School of Medicine. "Many system-level changes have been implemented to improve safety for patients in our medical workplaces. What we find in this study is that physician burnout levels appear to be equally, if not more, important than the work unit safety score to the risk of medical errors occurring."

The study was published online July 9 in the *Mayo Clinic Proceedings*. Shanafelt, who is also a professor of hematology and the Jeanie and Stew Ritchie Professor, is the senior author. Daniel Tawfik, MD, an instructor in pediatric critical care medicine at Stanford, is the lead author.

A national epidemic

Medical errors are common in the United States. Previous studies estimate these errors are responsible for 100,000 to 200,000 deaths each year. Limited research, though, has focused on how physician burnout contributes to these errors, according to the new study.

The researchers sent surveys to physicians in active practice across the United States. Of the 6,695 who responded, 3,574 — 55 percent — reported symptoms of burnout. Ten percent also reported that they had made at least one major medical error during the prior three months, a figure consistent with previous published research, the study said. The See BURNOUT, page 7

PR IMAGE FACTORY / SHUTTERSTOCK.COM

Physician burnout may be the source of even more medical errors than unsafe medical workplace conditions, according to researchers.

Magnetized wire could be used to detect cancer in people, scientists say

By Hanae Armitage

A magnetic wire used to snag scarce and hard-to-capture tumor cells could prove to be a swift and effective tactic for early cancer detection, according to a study by researchers at the School of Medicine.

The wire, which is threaded into a vein, attracts special magnetic nanoparticles engineered to glom onto tumor cells that may be roaming the bloodstream if you have a tumor somewhere in your body. With these tumor cells essentially magnetized, the wire can lure the cells out of the free-flowing bloodstream using the same force that holds family photos to your refrigerator.

The technique, which has only been used in pigs so far, attracts from 10-80 times more tumor cells than current blood-based cancer-detection methods, making it a potent tool to catch the disease earlier. The technique could even help doctors evaluate a patient's response to particular cancer treatments: If the therapy is working, tumor-cell levels in the blood should rise as the cells die and break away from the tumor, and then fall as the tumor shrinks.

For now, Sam Gambhir, MD, PhD, professor and chair of radiology and director of See WIRE, page 7

5 QUESTIONS

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

Ioannidis calls for more rigorous nutrition research

Pervasive and compelling though it may be, research on nutritional health frequently yields less-than-dependable results. This, at least, is the opinion of John Ioannidis, MD, DSc, professor of medicine and of health research and policy at the School of Medicine. He suggests that many of the studies that aim to collect information about what we put in our bodies and how it affects our health is flawed — too small, not randomized or otherwise biased in some way. Too often, findings from one study might contradict those of a similar study, and it stunts progress in the field, he believes.

In a perspective piece published online today in Advances in Nutrition*, Ioannidis and postdoctoral scholar John Trepanowski, PhD, suggest that a change is in order. Instead of many small, finely curated nutrition studies, the pair argue for a more robust approach in which scientists pool resources to answer big questions about nutritional health.*

To learn more about this vision, science writer Hanae Armitage spoke with Ioannidis about the current state of nutritional research; the feasibility of conducting large, randomized trials in the field; and what Ioannidis sees as the most important questions to pursue.

1 There seems to be a lot of contradictory findings related to nutritional research. What do you think is the main reason for that?

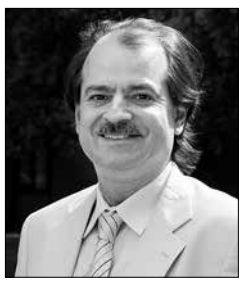
Ioannidis: We still largely depend on nonrandomized studies to assess questions of nutrition. These studies are notoriously incapable of giving reliable answers due to confounding factors. In nutrition, the situation is made even worse because our ability to measure diet is still limited in accuracy, and recall biases, in which study participants remember something incorrectly, can be severe. In addition, dietary intake of a single nutrient probably has small or even tiny effects on major health outcomes, even if diet as a whole is important. Therefore, any potential finding is largely shaped by the noise from errors and biases of observational studies.

2 What is the biggest inherent problem in the current designs of nutritional studies, and how do you think it could be remedied?

Ioannidis: The biggest problem is that the vast majority of studies are not experimental, randomized designs. Simply by observing what people eat — or even worse, what they recall they ate — and trying to link this to disease outcomes is moreover a waste of effort. These studies need to be largely abandoned. We've wasted enough resources and caused enough confusion, and now we need to refocus. Funds, resources and effort should be dispensed into fewer, better-designed, randomized trials.

3 Do you have a sense of how nutrition researchers feel about this approach?

Ioannidis: As you might expect, it's double-sided. Many doctoral and postdoctoral students are being trained to continue this pandemic of flawed designs and unreliable results. But at the same time, I think many other scientists in the field see the need for a paradigm shift.



John Ioannidis

4 How feasible would it be to implement a new approach to nutrition research in which resources are pooled for larger studies and a handful of major questions are pursued?

Ioannidis: It should be very feasible to implement this new approach. The cumulative cost would not be higher; it may even be less expensive. We would ask fewer questions, but we would get far more solid answers. We may be able to start getting some reliable evidence to inform nutritional guidelines rather than have them be battlefields of opinion.

5 What are some of the more pressing questions that you would hope to answer through these large, randomized trials?

Ioannidis: Any question that is relevant to pragmatic, real-life handling of diet and nutrients can be addressed with such trials. We can at last get some sense of whether one diet is best, or if they're all the same in terms of caloric intake. We can better assess specific nutritional or dietary strategies and more carefully parse the impact of health-policy decisions that are otherwise guided by special-interest parties and studies that are open to interpretation. In some cases, however, we don't simply want to see what people eat in real life, but we seek to answer questions of physiology or mechanism. In these situations, randomized trials with direct observation of participants in experimental in-house settings could support those goals.

Other options include registry-based designs, in which randomized trials are embedded in registries and are linked to all the information that is collected, and N-of-1 designs, in which single participants sequentially get randomized into different dietary options to get personalized assessments. Mendelian randomization designs may also help generate randomized trial equivalents using information from genetic markers. In all, we have a wide array of experimental design options that can address almost any question in nutrition far more reliably than we do now with nonexperimental data collections. **ISM**

Nicotine-mimicking drugs could help treat inflammatory diseases

By Bruce Goldman

Until the day that science identifies the precise genetic factors that allow some of us to live to be 100 despite the immensely damaging effects of inhaling the particulate byproducts of combusted plant biomaterials — also known as smoking — nobody should smoke. From any rational health care standpoint, it's a really bad idea.

But here's a dirty little secret of medical research: Nicotine — a highly addictive substance that keeps tobacco smokers hooked on the habit — has actually been shown to have therapeutic properties. Tobacco smoking has been demonstrated in numerous studies to have a negative association with Alzheimer's and Parkinson's diseases as well as with inflammatory bowel disease. It seems that nicotine — tobacco's pharmacologically active ingredient — is doing something right.

Nicotine acts directly on receptors located on certain kinds of nerve cells. In fact, an entire class of cellular receptors for the important nerve-cell signaling substance acetylcholine is designated as "nicotinic" just because receptors of this type respond to nicotine pretty much as they do to acetylcholine.

Nicotinic acetylcholine receptors come in several varieties. One, designated the alpha-7 nicotinic acetylcholine receptor, or alpha-7 nAChR, abounds on nerve cells in many distinct regions of the brain; defects in its function have been fingered in both Alzheimer's disease and schizophrenia.

Good guys or bad guys?

Here the plot thickens, quite literally.

In 2012, Larry Steinman, MD, professor of pediatrics and of neurology and neurological sciences at the School of Medicine, and Jonathan Rothbard, PhD, a senior scientist in Steinman's lab, along with their colleagues found that a sawed-off little protein by the name of beta-amyloid — possibly the most reviled molecule in the history of medicine because its buildup in the brain is frequently deemed the villain in Alzheimer's disease — had a therapeutic effect in a rodent model of multiple sclerosis. Supplying beta-amyloid to these animals actually reversed their paralysis, albeit only for the time during which it was being administered to them.

NORBERT VON DER GROEBEN

Larry Steinman and his colleagues discovered that a receptor that binds to nicotine and to clusters of beta-amyloid molecules is found on certain types of immune cells that can act as suppressors and regulators of the immune system.

Beta-amyloid is one of numerous proteins known to have biochemical properties that make it possible for them to stack together to form so-called amyloid fibrils, potentially thickening into gummy plaques. Among these amyloid-forming proteins are the infamous Alzheimer's disease-related proteins tau and beta-amyloid, which can form, respectively, neurofibrillary tangles and plaques in the brain and are believed by many scientists to be the cause of Alzheimer's disease. And there's the prion protein, infamous for mad cow disease and its rare but deadly equivalent in people.

In earlier studies, Steinman's lab had discovered that another amyloid-forming protein was therapeutic in an acute stroke model and that several additional amyloid-forming compounds could suppress immune hyperactivity.

But why?

It happens that the alpha-7 nicotinic receptor is also found on certain types of immune cells that can act as suppressors and regulators of the immune system. And, it turns out, a study published online June 18 in the *Proceedings of the National Academy of Sciences* shows that those amyloid-forming proteins can activate this receptor on these immune cells, resulting in a dialing down of inflammation. Steinman, who is also the George A. Zimmermann Professor, is senior author of the study and Rothbard is the lead author.

Bottom line: Alpha-7 nAChR-activating drugs might have therapeutic benefits in a variety of inflammatory diseases. Steinman and Rothbard are working to develop small-molecule therapeutics targeting this receptor that are safe for human use against rheumatoid arthritis, gout, inflammatory bowel disease and multiple sclerosis.

"As a neurologist and immunologist, I view this work as a thrilling connection between my two favorite physiologic systems," Steinman said. **ISM**

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STANFORD MEDICINE

Solved: Mystery of patient with suspected heart condition

By Tracie White

Although DNA testing is becoming increasingly quick, cheap and easy to perform, the results are sometimes ambiguous: Gene mutations called "variants of uncertain significance" can create uncertainty about a patient's risk for a disease.

"This is a really big problem," said Joseph Wu, MD, PhD, professor of cardiovascular medicine and of radiology at the School of Medicine. "If someone tells me I have a genetic variant that could cause sudden cardiac death, I'm going to be very scared. The result could be a lifetime of unnecessary worry for a patient when, in fact, the variant may be completely benign."

Now, Wu and a team of researchers have developed a technique that could shed light on the significance of such variants. In a new paper, they discuss how they used advanced genetic-editing tools and stem cell technology to determine whether a 39-year-old patient with one of these mysterious mutations was at increased risk for a heart-rhythm condition called long QT syndrome, which can cause erratic heartbeats, fainting and sudden cardiac death.

"This is one of the first cases of using stem cells and genomics for precision cardiovascular medicine," said Wu, who is also the Simon H. Stertzer, MD, Professor and director of Stanford's Cardiovascular Institute.

The paper was published June 26 in the *Journal of the American College of Cardiology*. Wu is the senior author, and Stanford postdoctoral scholar Priyanka Garg, PhD, is the lead author.

Heart palpitations, lightheadedness

The patient, who had a history of heart palpitations and lightheadedness, contacted a doctor worried about these symptoms. His family history showed he had a cousin who died of a heart attack playing soccer, a brother with a history of fainting and a grandfather who had four brothers die suddenly before the age of 40. A doctor ordered several electrocardiograms to test his heart function.

The results of those tests were cause for concern and, although ultimately inconclusive, his doctor chose to be cautious and prescribed the patient beta-blockers, a medication often used to treat mild cases of long QT syndrome. Genetic tests were inconclusive, as well, but showed the patient had a variant of uncertain significance on the KCNH2 gene. This was worrisome because several other mutations on this gene are known to cause long QT syndrome type 2, one of the most common types of the disorder.

The patient was referred to Wu and his colleagues, who set out to determine whether the variant was pathogenic or benign.

Their first step was to generate induced pluripotent stem cells — or iPS cells, which can develop into any type of cell — from cells obtained from the patient's blood. The iPS cells were differentiated into cardiomyocytes, or heart cells that actually beat spontaneously in the culture dish like a heart. They had the exact genetic makeup of the patient, including the variant of the KCNH2 gene.

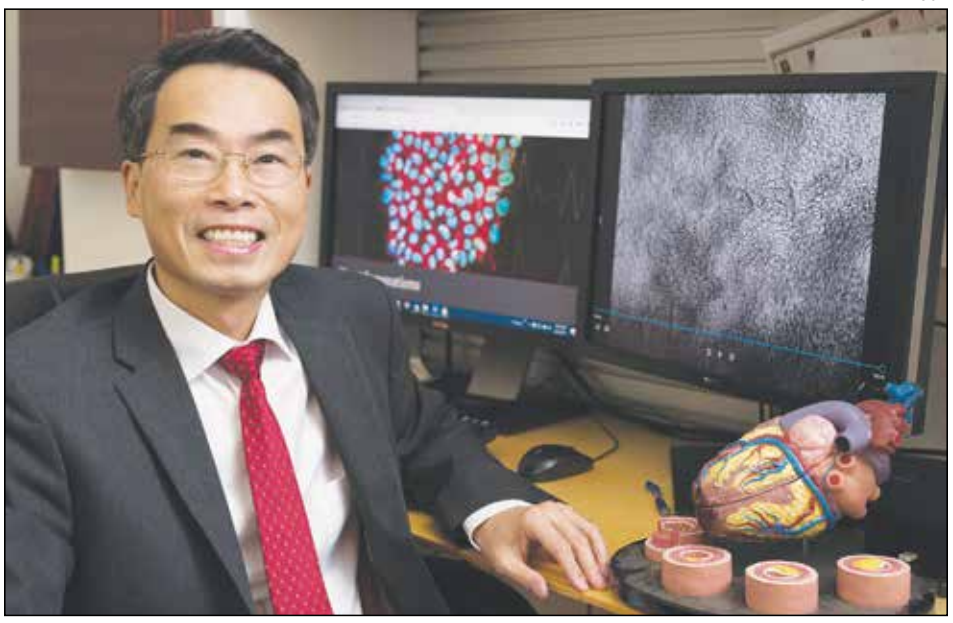
"You can generate a patient's heart cells in a dish and study them just from a simple blood sample."

These kinds of cells, which are grown in the lab, are what researchers refer to as a "disease in a dish" or a "patient in a dish." They can be used for a variety of tests, including many that may not be feasible to conduct on patients themselves. The researchers also developed heart cells from a healthy patient for comparison.

"An advantage of generating patient-specific iPS heart cells is that you don't have to use any invasive procedures on the patient to get them," Garg said. "You can generate a patient's heart cells in a dish and study them just from a simple blood sample."

The researchers used a gene-editing tool known as CRISPR to correct the mutation, a faulty nucleotide in the KCNH2 gene, and also to introduce the same faulty nucleotide into the healthy control gene.

STEVE FISCH



Joseph Wu and his collaborators used genetic-editing tools and stem cell technology to uncover whether a genetic mutation linked to a heart rhythm disorder was benign or pathogenic.

Tests of the heart cells with the mutation showed the hallmark features of long QT syndrome, including electrical disturbances that delay heartbeats and a mild propensity for arrhythmias compared with the cells from the healthy patient, the study said. These results did not show up in tests on the cells in which the mutation was turned off or in unaltered cells from the healthy patient.

The results confirmed that the patient did have a mild case of long QT syndrome, the study said.

In another study published recently in *Circulation* and also led by Wu, the researchers used the same genetic-editing tools and stem cell technology to determine that a variation of uncertain significance, which doctors worried could have been an indication of a dangerous heart condition known as hypertrophic cardiomyopathy, was actually benign.

"We were able tell the patient not to worry about it," Wu said.

The success of using these same methods to determine whether two different patients were at risk for two completely different diseases suggests that this platform is a promising risk-assessment tool for variants of uncertain significance in general, Wu said. "The results of these studies are particularly exciting to me because we used precision health methods to address an unmet need for a patient," he said. "This means we now have the ability to go deeper and tell a patient what a variant of uncertain significance means."

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

The study's other Stanford authors are instructors Angelos Oikonomopoulos, PhD, and Yingxin Li, PhD; former postdoctoral scholar Haodong Chen, PhD; postdoctoral scholar Chi Keung Lam, PhD; Karim Sallam, MD, clinical assistant professor of cardiovascular medicine; and Marco Perez, MD, assistant professor of cardiovascular medicine.

Researchers from the University of Utah also contributed to the study.

The research was funded by grants from the National Institutes of Health and the American Heart Association.

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

Virtual athletes compete to take on a medical challenge

By Nathan Collins

The contestant wastes no time. It swings a prosthetic leg violently forward, drags its other leg quickly behind, then collapses into the ground — but it's okay. This athlete is computer-generated, and what its creators learn from its fall could help them win a contest with a serious goal: designing better prosthetic limbs and helping patients adapt to them.

Łukasz Kidziński, PhD, a postdoctoral scholar in bioengineering, cooked up the contest following the success of a similar event last year in which teams of academics, private-sector artificial intelligence researchers and enthusiasts competed to train virtual athletes to run through an obstacle course.

That first online contest stemmed from a basic problem Kidziński and his colleagues faced. While researchers like his adviser, Scott Delp, PhD, professor of bioengineering and of mechanical engineering, know a great deal about how bones and muscles move, no one is quite sure how the brain controls complex processes like walking and running.

To close that gap, Kidziński hit on the idea of a competition, in which teams from around the world would compete to design artificial intelligence algorithms that would, along with virtual bodies informed by Delp's data and models, learn to walk, run and eventually navigate obstacles. The winning algorithms, the researchers believed, could tell them something about how real people would learn to walk and run — or more to the point, how they would relearn to walk and run after surgery, although the first contest did not directly address that issue.

'A big step forward'

This year, he aimed higher.

"Last year was more of a proof of concept," Kidziński said. "This year we want to get closer to medical applications."

In this year's version, teams now work with a virtual body that includes a prosthetic leg, with the aim being to understand how people would learn to move again after losing a limb and gaining a protheses. Although no contestant has made it very far yet — teams are judged on how far their virtual competitors can walk from a starting point — Kidziński isn't worried. Last year around this time, no team had managed more than walking a few steps, and some fell flat on their faces, virtually speaking.

"Compared to the first challenge, this new challenge is a big step forward."

"It wasn't obvious the problem would be solved," Kidziński said, but solved it was. Although last year's winner was perhaps not the most elegant runner, it made it through an obstacle course, in the process showing the approach could work.

"Compared to the first challenge, this new challenge is a big step forward," Kidziński said, but still he expects it will be solvable, not to mention enticing. Last year, the contest attracted 442 teams. Three weeks into this year's contest, 100 teams have signed up to participate and made more than 500 entries so far.

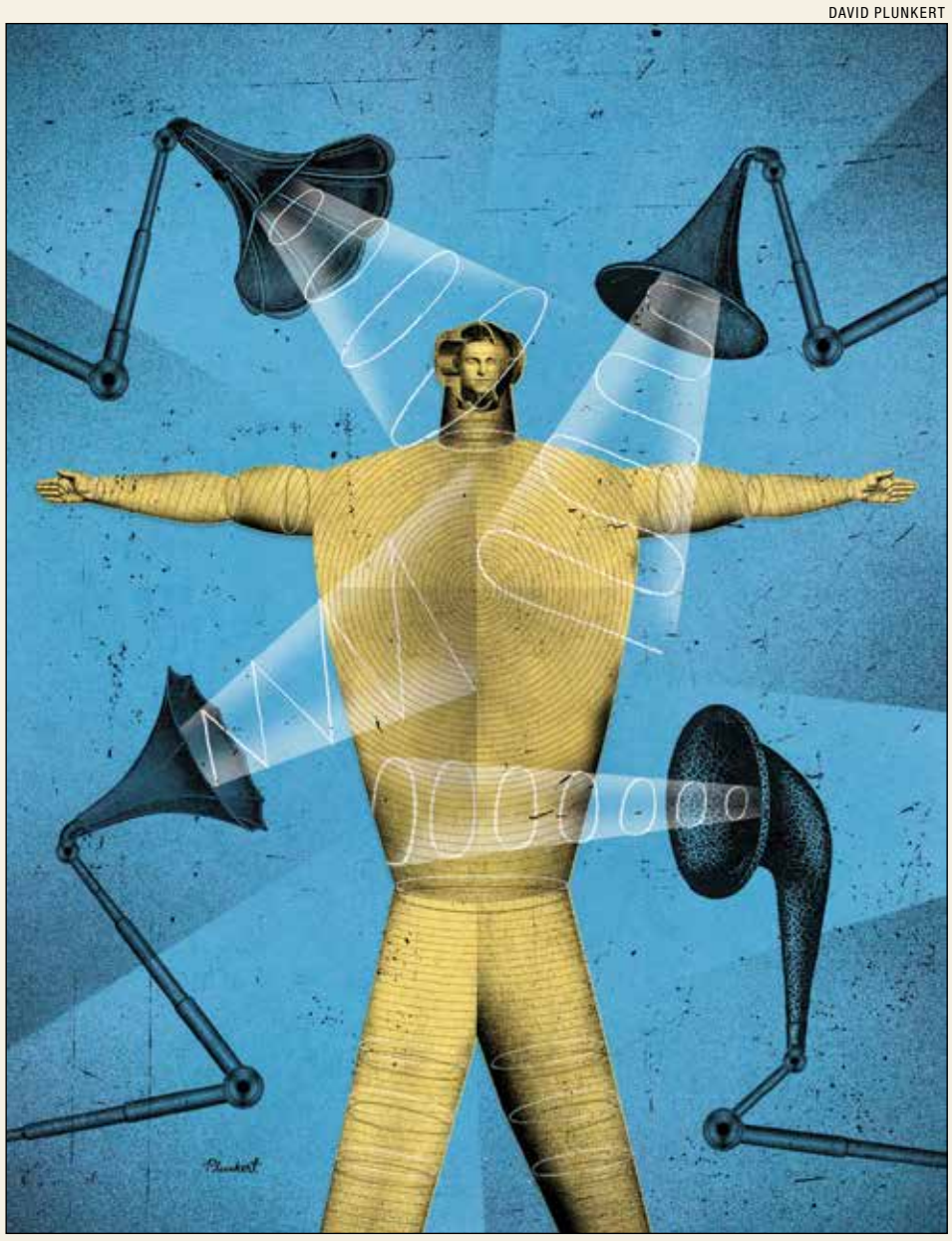
After last year's success, Kidziński hopes to get upward of 1,000 participants, in part through expanded incentives. This year, Nvidia will award its top graphics-processing units to the top three teams, and Google has offered cloud computing resources for teams who might otherwise find it difficult to take part.

But most important, Kidziński said, is that what was once a crazy idea — crowdsourcing algorithms to solve problems in biomechanics — has worked out so well that it could one day go from a virtual contest to helping real people in the real world.

Details on how to participate, including information on free resources to get started, are available at https://www.crowdai.org (click on the link titled "NIPS 2018: AI for Prosthetics Challenge"). ISM

Stanford scientists harness noise, acoustics for better health

DAVID PLUNKERT



By Hanae Armitage

From the original stethoscope, invented more than 200 years ago, to the fleeting chirp of gravitational waves, sound has reverberated throughout the history of technological and scientific advances.

Today, the role of sound in science extends beyond the range of audible frequencies: Ultrasonic and other silent acoustic waves have made their way into researchers' repertoire, helping them push the boundaries of conventional medicine and research.

In examples from four Stanford labs, scientists are investigating the full spectrum, harnessing the nuances of noise and the power of acoustics to generate inventive, if not unexpected, technologies that show just how potent the combination of sound and science can be.

Acoustic choreography

Heart cells are among the most densely packed in the body: About 100 million fit into a space the size of a sugar cube. The compact structure crams the cells so close together that they can communicate with one another and beat as one lump. For tissue engineers, however, it poses a tricky hurdle: Pack the cells too tightly and some won't get proper nutrients; too loosely, and they can't coordinate a beat.

Cardiologist Sean Wu, MD, PhD, had been probing the problem when he met Utkan Demirci, PhD, an acoustic bioengineer and professor of radiology. "Utkan brought up this idea that we could use acoustics to pack the cells very densely and still maintain an ability to control and tune their organization — and we got really excited," said Wu, associate professor of medicine.

Sean Wu

Utkan Demirci

Demirci's idea exploits a type of acoustic signal that creates Faraday waves, which result from a physical perturbation at the interface of liquid and air. (If you've ever flown in a turbulent plane with a beverage, you've witnessed Faraday waves in your cup). The waves cause ripples in the liquid, and anything floating in the liquid sloshes around, too.

"You can trigger those ripples on the microscale," Demirci said. "Like when the tides of the ocean sweep a sunken ship's treasures to shore — we're sort of doing the same thing with heart cells." The big difference, however, is that Demirci and Wu can control the "swell" by tuning a knob that changes the waves.

Wu and Demirci can then shepherd the heart cells into nearly any pattern they want. "You can make triangles, hexagonal shapes, circles, lines — you can even make a little human shape," Demirci said.

Wu added, "If you don't like the pattern, for whatever reason, you can change it, literally, within five or six seconds. You change the frequency and amplitude, and the cells move into a new spot right in front of your eyes."

Unlike other tissue-engineering tactics, acoustics position the heart cells in a tight configuration that closely resembles natural cardiac tissue, turning the resulting, beating blob into something valuable for medicine.

Wu and Demirci think acoustic engineering could help foster more realistic cardiac disease modeling and drug screening. More distantly, but still on the horizon, the pair even see their generated tissue as an option for heart patches in patients who have weak cardiac walls or have damage from a heart attack.

Demirci and Wu said that they plan to add vascularization — conduits that carry blood and oxygen to various parts of an organ — to make their generated heart tissue even more realistic.

The buzz

Nothing incites irritation in quite the same way as a lurking mosquito. But its high-pitched drone may actually help curb spikes in mosquito populations and, more importantly, the diseases that they pass on to humans. This, at least, is the premise behind Manu Prakash's newly launched app, Abuzz.

Prakash, PhD, assistant professor of bioengineering, supervised a team that created Abuzz to digitally identify and tag mosquito species based on their hums. His vision: build a "soundscape" that maps the global whereabouts of these voracious vectors and provide details about the diseases they can carry — Zika, malaria, dengue and the like. It may seem lofty, but Prakash asserted that all he needs is an avid user base with access to cellphones. ("Dumb" phones like a flip phone also make the cut.)"Our goal is to put the data in the hands of locals and public health organizations who are focused on mosquito-disease elimination," Prakash said. "We want this to provide details of mosquito ecology — species, associated diseases, the location of the recording — so that it can be a worldwide awareness and alert system for disease-carrying mosquitoes."

Naturally, populating such a map will take time, and a lot of users. So how does one collect that much data from far-flung corners of the globe? Recruitment and a simple training session, Prakash said, that consists of four basic steps: venture out, creep up to a mosquito (or let it creep up to you), record its pitchy hum and send the data to Abuzz for analysis.

KURT HICKMAN

Felix Hol and Haripriya Mukundarajan with Manu Prakash, whose lab has created an app called Abuzz that he hopes will help produce a detailed global map of mosquito distribution.

Abuzz — the Shazam app of the insect world — uses software to determine if the recorded noise is really a mosquito, not a house fly, distant jet or other imposter. Then, it compares the recording with a database of different mosquito buzzes and tries to find a match. This is possible because every mosquito species emits a unique sound, generated by the flutter of its wings.

Ideally, knowing the geographic regions where specific mosquito species are recorded can help battle unwanted multiplication. "Locals could look in their neighborhood for likely mosquito-spawning areas and remove the larvae," Prakash suggests.

Or, on a larger scale, agencies that try to hinder populations by releasing genetically modified mosquitoes could use the information to more precisely target regions and species. (Releasing an army of mosquitoes into the ether may sound rather vile, but gene modifications in these mosquitoes make their offspring unviable, helping to curtail a climbing population.)

"What's beautiful about Abuzz is it's not just limited to mosquitoes," Prakash said. "Right now, we're looking into whether we can use this method to identify sick versus healthy honeybees." They don't have the answer, but as the health of honeybees in the United States continues to decline, Prakash and his team hope that their platform can help reveal the biology behind more than one flying insect.

A symphony in the brain

While listening to a string quartet play over recordings of plasma waves captured in outer space and converted into sound, neurologist Josef Parvizi, MD, PhD, dreamed up a symphony of his own. If you can turn signals from space into sound, perhaps you could turn brain waves into sound too, he thought.

So Parvizi sent an out-of-the-blue email to Christopher Chafe, a composer with expertise in converting atypical data sets into music, and explained his vision. Parvizi, professor of neurology, describes what happened next: "A crazy music professor and a crazy neurologist decided to collaborate on a strange idea." Chafe is the director of Stanford's Center for Computer Research in Music and Acoustics.

After several years of refining, the idea developed into something that Parvizi has dubbed the brain stethoscope.

The instrument, which is noninvasive and looks like a sweatband, straps onto a person's head and listens to the brain's electrical signals. With a push of a button, those signals are converted to sound that streams from a small speaker connected to the band. The thought is that doctors can "hear" the tone of the brain — particularly if there is a seizure.

"Imagine that you open a hotel room window and the entire town is chanting

NATIONAL INSTITUTES OF HEALTH

Christopher Chafe and Josef Parvizi collaborated on a device that converts the brain's electrical signals into sound.

exactly the same thing," Parvizi said. "You may not know exactly what's happening, but you know it's not normal. It's the same idea with the brain; you don't want signals to be too synchronous. If they are, the brain is having a seizure." It turns out, the audible difference between a seizing brain and a normal brain is quite distinct; almost anyone can hear it.

Of course, Parvizi acknowledged, if someone is convulsing and shaking, you don't need a stethoscope to tell you they're having a seizure. "But there's such a thing as 'nonconvulsive subclinical seizures,' and those don't have the obvious physical symptoms."

But they still have some subtle symptoms. Someone having one of these silent storms might appear disoriented and nonresponsive, or they might fall asleep suddenly. In the public eye, this type of seizure more often flies under the radar, but that's not to say they're less threatening to health. Parvizi said there's now a stockpile of evidence showing that prolonged silent seizures are damaging to the brain, especially in children, whose brains are still developing.

"Right now, patients need a trained neurologist to detect a seizure," he said. "It may be controversial, but my goal is to enable anyone to detect them — all kinds of physicians, nurses, medical trainees."

Even parents.

"You want moms and dads to be able to know if their kid is having a seizure so that they seek out professional attention," Parvizi said.

In May 2017, the Food and Drug Administration gave the green light to Parvizi's invention, and he has since tested the stethoscope's capabilities in several hospitals, finding encouraging results.

"This could change health care dramatically when it comes to monitoring brains," he said.

Powering implantable medicine

Place two grains of rice next to each other and you've about replicated the size of a rather savvy, next-generation medical chip devised by Amin Arbabian, PhD, assistant professor of electrical engineering. The chip is an implantable device, like a pacemaker or nerve stimulator, but is set apart by the way it's powered — not by batteries or wires, but by sound.

"It has been a long-standing challenge to make medical devices as small as possible and operate deep in the body," said Arbabian. "Ultrasound enables that."

Ultrasound's long-term use in fetal imaging has earned it a reputation in medicine for being safe and dependable, making it a prime candidate to power a chip that can be embedded in the body. Perhaps equally as important, the gentle sound waves also support versatility. A Swiss army knife of implantable devices, the chip can change its function to fulfill different biological needs. Its various modes are controlled by the same thing that fuels it. "Ultrasound is both a power source and a way to communicate with the device," Arbabian said.

A tiny module, called a harvester, sits on the chip and converts ultrasound waves into electrical energy. By beaming pulses of ultrasound to the chip, Arbabian can send encoded commands, like Morse code. "We can, for example, instruct it to start monitoring a certain parameter, like blood pressure, or channel an electrical pulse to stimulate a nerve or trigger the precise release of a drug at a particular location," he said.

The goal, he said, is to create an active "smart" chip or a distributed network of smart chips to not only execute specific commands, but also to monitor physiological parameters and transmit useful data about a patient. This information, on such things as insulin levels or blood pressure, would be sent to an external device, where doctors could access it. In that vein, Arbabian and his lab team are working toward a closed-loop system in which the implant is self-sustaining and can run seamlessly in the body, without constant instruction.

In a closed-loop system, the chip's sensors would trigger the release of a dose of its therapeutic agent, which could be an electrical pulse or a drug enclosed in a separate chamber of the chip. In patients with hypertension, for instance, the implant would monitor the arteries. If the chip sensed increased blood pressure, it would administer a drug to help bring the pressure down.

"We could see this system working for maintaining blood pressure, or managing urinary incontinence or diabetes," Arbabian said.

ROD SEARCEY

Amin Arbabian devised an implantable medical chip that is powered by ultrasound waves it converts into eletrical energy.

He and his team are working on the next generation of the implant and partnering with other labs to test their setup in animals. They even have a research collaboration with the FDA, which is independently investigating the prototypes.

"There's a lot more work to be done," Arbabian said. "But there's a lot of reason to be hopeful." ISM

Disease inspires team to develop test for aldehyde levels in blood

By Nathan Collins

During the first 10 years of their lives, kids born with Fanconi anemia lose the ability to make blood cells and need bone marrow transplants to survive. And although the transplant cures the bone marrow failure, people remain at greatly increased risk of cancer and rarely live past their 20s.

Unfortunately, there are no drugs to treat the underlying cause of Fanconi anemia, which is thought to be DNA mutations induced by molecules called aldehydes.

Part of the problem in developing a cure comes down to an inability to measure aldehydes in the blood. But that might be about to change, thanks to an interdisciplinary collaboration aided by a grant from Stanford ChEM-H.

Kenneth Weinberg

Eric Kool

"If we had a drug and we were doing clinical testing, we would love to be able to say, 'Here's your aldehyde level before you started the drug, and here are the aldehyde levels in your blood cells after you started the drug,'" said Kenneth Weinberg, MD, a professor of pediatrics.

If successful, such a test could help in developing a treatment to stop the aldehyde-induced DNA damage in people with Fanconi anemia and also help millions who are at risk of aldehyde-related cancers because of common genetic mutations or industrial exposure.

Not just a curiosity

Many aldehydes occur naturally. They are what gives ripening peaches their pleasant smell. One aldehyde, acetaldehyde, is what causes around 8 percent of people — and one-third of East Asians — to flush when they drink alcohol.

But over the past decade, researchers have learned that in some cases aldehydes can cause strands of DNA to become tangled, preventing them from producing essential proteins and from replicating properly. In the worst cases, that tangling kills blood-forming stem cells in patients with Fanconi anemia. These patients lack genes needed to unravel and repair the tangled DNA.

"I think many people have thought this mutation is just a curiosity."

This DNA damage is behind a number of cancers as well. The mutation in people from East Asia, for example, prevents the body from breaking down acetaldehyde and increases the risk of esophageal cancer by about a factor of 70, Weinberg said.

"I think many people have thought this mutation is just a curiosity: 'Here's someone who, if they have a drink of alcohol, gets flushed, nauseated, headache, feels terribly ill, so they don't drink alcohol,'" said Weinberg, who holds the Anne T. and Robert M. Bass Professorship in Pediatric Cancer and Blood Diseases. "I'm beginning to look at it as a pre-disease state rather than a curiosity."

Testing for peach smell

Despite the growing understanding of Fanconi anemia and the role aldehydes play in promoting cancer, there are as yet no drugs to eradicate the molecules, in large part because they are as ephemeral as the smell of peaches. In other words, they evaporate too easily. As a result, conventional blood tests don't pick them up, so researchers like Daria Mochly-Rosen, PhD, a professor of chemical and systems biology who collaborates with Weinberg, can't tell if her efforts to create aldehyde-busting drugs are doing any good.

At the suggestion of Mochly-Rosen, who also holds the George D. Smith Professorship in Translational Medicine, Weinberg went to chat with chemistry professor Eric Kool, PhD, a few years back. About half an hour in, Weinberg said, Kool had sketched out the idea for what would become Darkzone, a chemical that glows brightly in the presence of aldehydes.

Kool, Weinberg and their collaborators published their first results on Darkzone in 2016. Now the aim is to improve on their existing results and take the method to the clinic, where they can begin testing it on people. The challenge is twofold, said Kool, who is also the George A. and Hilda M. Daubert Professor in Chemistry. First, they want to improve Darkzone's light output, so that it will be easier to see how much aldehyde is present in a blood sample.

Second, the team will need to develop blood-drawing equipment that maintains a consistent vacuum and prevents aldehydes from escaping the blood samples. The researchers are modifying an existing device that, rather than drawing blood from a vein, sucks blood through the skin with several hundred tiny needles. That blood could then be fed into a vacuum-sealed device preloaded with Darkzone.

Beyond disease and mutations

The principle aim, Weinberg said, is to help develop better drugs for Fanconi anemia and aldehyde-related cancers.

But there is another, perhaps equally important application down the road. Aldehydes — including formaldehyde and acetaldehyde — are everywhere. "Right now, you're sitting at a laminated wooden desk and you are breathing in small amounts of acetaldehyde," Weinberg said. The chemical is prevalent in plywood, paint and electronics.

And if it's bad for those of us sitting at laminated wooden desks, it's worse for those who make those products, especially in countries — many in East Asia, no less — where aldehydes are less tightly regulated. "Aldehydes are industrial toxins, so it would be fantastic if we had the ability to measure people's exposure and use that to drive efforts to mitigate their exposure to these chemicals," said Weinberg, a member of Stanford Bio-X, the Child Health Research Institute, and the Stanford Cancer Institute

Kool is also a member of Bio-X, the Child Health Research Institute, the Stanford Cancer Institute and Stanford ChEM-H. Mochly-Rosen is also a member of Bio-X, the Cardiovascular Institute, the Child Health Research Institute, the Stanford Cancer Institute, Stanford ChEM-H, and the Stanford Neurosciences Institute. ISM

Program

continued from page 1

in the program. At least half of the teens in the program are away from home for the first time.

Group activities at the residence facilitate bonding. "We have identity workshops; '*todos* time,' where everyone responds to a question; and storytelling," said Luis Arreola, 18, a rising sophomore at Stanford and a program counselor. Arreola, from El Sobrante, California, is an alumnus of the 2015 program. "All these activities push the participants out of their comfort zone. They become closer, more authentic and — it's almost as if you knew these people your entire life."

The close, community experience is especially important for students coming to the program with big goals complicated by challenging backgrounds. "This is a program for students who are low-income, who often experience high levels of adversity. And for counselors, it's not just a summer job," said Shorter, who was a counselor herself in in the program in 2008, following her sophomore year at Stanford. "It's a transformative experience for counselors, too, many of whom come from a similar background and see that a mentor really changed their lives, and they want to now do that for someone else."

STEVE FISCH

Homar Murillo (wearing glasses), a 17-year-old student at Leadership Public High School in Hayward, California, wants to be a trauma surgeon.

Tracking the program's alumni

Among students who fail to complete high school in California, the vast majority — 80 percent — are low-income, according to a 2018 report from Johns Hopkins University. Close to 100 percent of participants in the Stanford Medical Youth Science Program graduate from high school, and just over 80 percent graduate from a four-year college. "We've been tracking alumni since day one," Shorter said. "More than 50 percent of our students either enter the health professions or go on to advanced graduate degrees and ultimately enter careers as clinicians or in other areas of health. As part of our 30th year, we're going to do a new, five-year longitudinal assessment."

The rigorous selection process for counselors begins about a year before the start of the summer program, and involves an application, multiple group interviews, behavioral interviews and a 10-week course taught by Shorter on leadership in multicultural health.

The criteria for the participating high school students are selective, but aren't focused solely on academic achievement. "We're looking for students who are ready to dive in deep," Shorter said. "And we know that might not mean the highest GPA. We're really asking them, 'What do you see in your community that you want to change, and how are you already taking those steps?' 'How are you already getting involved in this world outside of just your coursework?' We're looking for their academic potential from a bigger picture above their test scores."

Homar Murillo, a rising senior from Leadership Public High School in Hayward, developed an interest in medicine while being treated during childhood for multiple health issues. Today, Murillo, 17, is healthy and grateful to the medical teams who helped him along the way. He's determined to become a trauma surgeon.

His school counselor suggested the Stanford program to him. "I expected study, study, study, study, and no one talking to each other," Murillo said. "But you walk into these doors and it's like you have a whole new family. I've never gotten so close to people as I have in this program. I haven't had so much academic support with people I barely know."

For Jasmine Dilworth, 17, a rising senior at Sunnyside High School in Fresno, the program presented a chance to accelerate her learning and test the waters at her dream school, Stanford. "Getting into this program really opened my eyes. I realized that I actually do have a lot of potential," Dilworth said.

For students like Murillo and Dilworth, the opportunity to experience anatomy labs with human cadavers was a compelling aspect of the program. Working with a cadaver was "nothing like I expected," Dilworth said. "But it was just really cool to apply what we learned that day to a real human body."

STEVE FISCH

(From left) Medical student Pablo Romano with Sujeiri Venegas, Monse Andrade and Ashlee Agundiz, who are among the program's 24 participants this summer.

Learning about the thorax and lungs

The first week's curriculum included study of the thorax and lungs in lecture, as well as in the anatomy laboratory and in Stanford Hospital with patients. "They took us into one of the rooms where the patient was getting the liquid in the cavity under his lungs removed," Dilworth said. "Then, later in the day we were talking about the lungs and the thoracic cavities. So it was just really interesting to apply the stuff that we've seen to an actual lesson, and to understand that it actually happens on a daily basis."

"We're looking for students who are ready to dive in deep."

During the program's five weeks, the students break into seven teams and develop research projects on health disparities. Projects this year include "Liver cancer within the Latinx community," "Obesity rates in Native American communities" and "Prevalence of substance abuse in the LGBTQ Latinx population."

"At graduation, each group shares their research project in a seven-minute presentation to a large audience of family, faculty and mentors," said program manager Grayson Throckmorton, a rising Stanford senior. "We also develop the research into a published form that they send to their policymakers at home."

What each student can bring back to their communities is an immediate benefit of the program, Shorter said. "We can only touch 24 lives each summer," she said. "But the students take home so much. They're changing their communities the day they go home. It doesn't just happen years from now when they become doctors. We don't have to wait for them to be leaders. They are leaders right this very second."

Now, Shorter and her team are looking ahead to the future. "Students who are 10 years down the road, they're going to continue to experience barriers," she said. "And the support that they need is very different from when you're 17 to when you're 27. This year we're launching our alumni association. How we can better support our alumni as they continue on their trajectory is at the top of the list of our priorities."

Winkleby still attends the first day of every summer session and stays involved with many former students for years after they finish the program, supporting alumni as they navigate the academic and professional worlds.

"When I came to Stanford, given my background, I had to learn to walk in the world of Stanford. And that was challenging. We're empowering these students to know that you can walk in both worlds," Winkleby said. "We're empowering them to know that they're smart, they belong in college and we need them in health careers."

Winkleby received grants during the program's early years to cover its annual costs of $100,000. In 1998, the program received funding for five years from Stanford Graduate School of Business alumnus Leo Hindery Jr. and three of his friends: John Malone, David Perry and John Doerr. The Edmund W. Littlefield Foundation also provided significant funding for several years. Then, in 2011, Hindery made a $500,000 endowment to the program, increasing it in 2016 with an additional $400,000. Stanford University and the School of Medicine also provide support. **ISM**

COURTESY OF CLARK/MCCARTHY

Strong minds, strong bodies, hard hats

Twice a week, members of the project team for the new Stanford Hospital take a break from work to practice yoga together. Participation helps lower stress levels and keeps the team working well together, said Mike Lipton, senior vice president of operations at McCarthy Building Companies. Lipton, who has been practicing yoga for nine years, leads the sessions, which are usually held mid-morning. "Yoga is about doing what you can do with your body," he said. "It is not a competition." The new hospital is scheduled to open in late 2019.

Wire

continued from page 1

the Canary Center at Stanford for Cancer Early Detection, is focused on the wire as a cancer-detection method, but its reach could be much broader.

"It could be useful in any other disease in which there are cells or molecules of interest in the blood," said Gambhir, who developed the wire with the help of his colleagues. "For example, let's say you're checking for a bacterial infection, circulating tumor DNA or rare cells that are responsible for inflammation — in any of these scenarios, the wire and nanoparticles help to enrich the signal, and therefore detect the disease or infection."

No vial of blood necessary

The study was published online today in *Nature Biomedical Engineering*. Gambhir is the senior author. Postdoctoral scholar Ophir Vermesh, MD, PhD; surgery resident Tianjia Jessie Ge, MD; and MD-PhD student Amin Aalipour share lead authorship.

Cells that have sloughed off the tumor and cruise the bloodstream freely, otherwise known as circulating tumor cells, can serve as cancer biomarkers, signaling the presence of the disease.

Why then, you might wonder, would you need an entirely new way to capture cells milling about the blood? Couldn't a simple blood draw siphon off the same floating tumor cells? Hypothetically, yes, but circulating tumor cells are often scarce, and a blood draw only samples a few milliliters of the total blood volume, which in adult humans is about 5 liters.

"These circulating tumor cells are so few that if you just take a regular blood sample, those test tubes likely won't even have a single circulating tumor cell in them," said Gambhir, the Virginia and D.K. Ludwig Professor of Clinical Investigation in Cancer Research. It would be like searching for a grain of sand in a bathtub, but only scooping out a few cups of water.

"So doctors end up saying 'Okay, nothing's there.'"

That, Gambhir said, is where he sees the magnetic wire making a difference. For the wire, which is about the length of your pinky finger and the thickness of a paperclip, to work, circulating tumor cells must be effectively magnetized with nanoparticles. The nanoparticles contain an antibody that latches onto circulating tumor cells. Once the floating tumor cell and nanoparticle are hitched, the cell lugs the tiny magnet around with it, and when the cell-magnet complex flows past the wire, it's compelled by magnetic force to veer from its regular path in the bloodstream and stick to the wire. Then, the wire is removed from the vein, and the cells are stripped for analysis.

Gambhir and his team have yet to try out the wire in people, as they still have to file for approval from the Food and Drug Administration, but they have successfully tested it in pigs, placing the device in a vein near the pig's ear. That vein is fairly similar to veins in the human arm. When compared with a 5-milliliter blood sample, the magnetic wire extracted 10-80 times more cancerous cells; compared with a different, commercially available wire-based detection method, the wire picked up 500 to 5,000 more tumor cells.

"We estimate that it would take about 80 tubes of blood to match what the wire is able to sample in 20 minutes," Gambhir said. Of course, he continued, it's not practical to remove 80 test tubes of blood from one person; that's more than a half-liter. "So, we're hoping this approach will enrich our detection capability and give us better insight into just how rare these circulating tumor cells are, and how early on they exist once the cancer is present."

A flexible wire

Gambhir said the technique could also be used to gather genetic information about tumors located in hard-to-biopsy places or to provide information about the efficacy of a cancer treatments. Perhaps most intriguingly, the magnetic wire may even stand to evolve into a treatment in and of itself.

"If we can get this thing to be really good at sucking up cancer cells, you might consider an application where you leave the wire in longer term," Gambhir said. "That way it almost acts like a filter that grabs the cancer cells and prevents them from spreading to other parts of the body."

Now, Gambhir is working to ready the technique for humans, which involves approval for the nanoparticles. His lab is conducting toxicity studies in mice, paying close attention to what happens to leftover nanoparticles that don't bind. So far, there are no signs of toxicity, and the extras decay over the course of a few weeks, he said. Gambhir is also looking into nanoparticles that are already FDA-approved, working to tweak them for use with the wire. Once the technology is approved for humans, the goal is to develop it into a multi-pronged tool that will boost detection, diagnosis, treatment and evaluation of cancer therapy.

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

The study's other Stanford authors are veterinary research coordinator Yamil Saenz, DVM; former graduate students Chin Chun Ooi, PhD, and Yue Guo, PhD; radiology and molecular imaging scientist Israt Alam, PhD; senior research scientist Seung-min Park, PhD; graduate student Charlie Adelson; postdoctoral scholars Hamed Arami, PhD, and Yoshiaki Mitsutake, PhD; assistant professor of comparative medicine Jose Vilches-Moure, DVM, PhD; life science technician Elias Godoy; research scientist Michael Bachmann, MD, ScD; preclinical laboratory managing director Jennifer Lyons; instructor of radiology Kerstin Mueller, PhD; life science technician Alfredo Green; Shan Wang, PhD, professor of materials science and engineering and of electrical engineering; and chemistry professor Edward Solomon, PhD, who is also a professor of photon science at SLAC National Accelerator Laboratory.

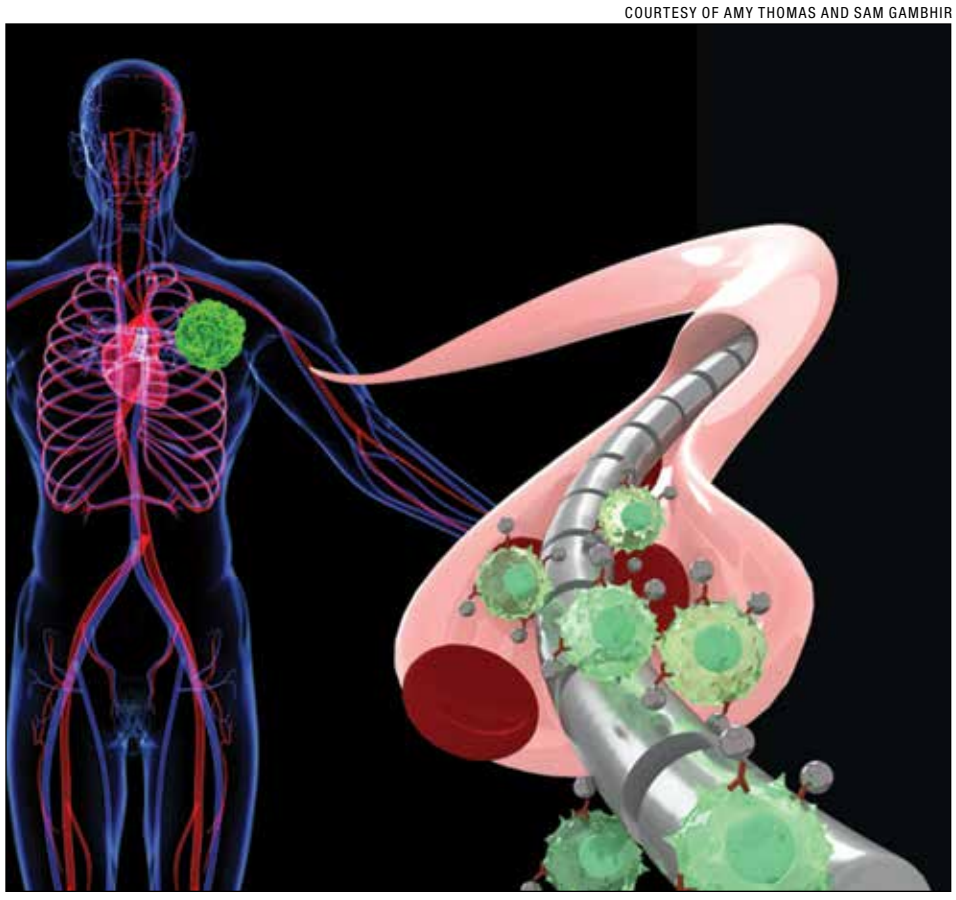
Gambhir is a member of Stanford Bio-X, the Stanford Cardiovascular Institute and the Stanford Neurosciences Institute.

The study was funded by National Institutes of Health, the Canary Foundation and the Ben and Catherine Ivy Foundation.

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

STEVE FISCH

COURTESY OF AMY THOMAS AND SAM GAMBHIR



Sam Gambhir (top) and his colleagues have developed a technique that employs a magnetized wire to capture free-floating tumor cells in the blood. (Bottom) If approved for use in humans, the magnetic wire (depicted in gray) would be inserted into a vein in the arm (light pink) and attract floating cancer cells labeled with magnetic nanoparticles (light green and gray) that have come from the tumor (neon green).

Burnout

continued from page 1

physicians were also asked to rank safety levels in the hospitals or clinics where they worked using a standardized questionnaire to assess work unit safety.

"We found that physicians with burnout had more than twice the odds of self-reported medical error, after adjusting for specialty, work hours, fatigue and work unit safety rating," Tawfik said. "We also found that low safety grades in work units were associated with three to four times the odds of medical error."

Tait Shanafelt

Daniel Tawfik

Shanafelt said, "This indicates both the burnout level as well as work unit safety characteristics are independently related to the risk of errors."

Physician burnout has become a national epidemic, with multiple studies indicating that about half of all doctors experience symptoms of exhaustion, cynicism and feelings of reduced effectiveness. The new study notes that physician burnout also influences quality of care, patient safety, turnover rates and patient satisfaction.

"Today, most organizations invest substantial resources and have a system-level approach to improve safety on every work unit. Very few devote equal attention to address the system-level factors that drive burnout in the physicians and nurses working in that unit," Shanafelt said. "We need a holistic and systems-based approach to address the epidemic of burnout among health care providers if we are truly going to create the high-quality health care system we aspire to."

The study also showed that rates of medical errors actually tripled in medical work units, even those ranked as extremely safe, if physicians working on that unit had high levels of burnout. This indicates that burnout may be an even a bigger cause of medical error than a poor safety environment, Tawfik said.

"Up until just recently, the prevailing thought was that if medical errors are occurring, you need to fix the workplace safety with things like checklists and better teamwork," Tawfik said. "This study shows that that is probably insufficient. We need a two-pronged approach to reduce medical errors that also addresses physician burnout."

In addition to their effect on patients, both errors and burnout can also have serious personal consequences for physicians. "We also know from our previous work that both burnout and medical errors independently double the risk of suicidal thoughts among physicians," Shanafelt said. "This contributes to the higher risk of death by suicide among physicians relative to other professionals."

Jochen Profit, MD, associate professor of pediatrics at Stanford, and researchers at the Mayo Clinic also contributed to the study.

The work was supported by the National Institutes of Health, the Jackson Vaughan Critical Care Research Fund, the Mayo Clinic Program on Physician Well-Being and the American Medical Association and the Mayo Clinic Program on Physician Well-Being.

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

New president, CEO of Lucile Packard Foundation for Children's Health appointed

Cynthia Brandt Stover, PhD, has been appointed president and CEO of the Lucile Packard Foundation for Children's Health, effective Sept. 4.

Brandt Stover has been campaign director at the Smithsonian Institution since 2013. She brings more than 20 years of experience in fundraising, campaign leadership and external relations to her new role.

"We are thrilled to welcome Cynthia to the foundation," said board chair Elaine Chambers, who served on the search committee led by board vice chair Manuel Henriquez. "With her remarkable successes in fundraising and her passion for the mission of children's health, she brings the perfect combination of skills and qualities needed to lead us to further success."

Brandt Stover will lead a 98-member staff. The foundation directs all fundraising for Lucile Packard Children's Hospital Stanford and for the maternal and child health programs at the Stanford University School of Medicine. Fundraising totaled more than $163 million last year. The foundation also operates a grant-making program aimed at improving health care systems for children with special health care needs, and kidsdata.org, a website that provides data about the health and well-being of children statewide.

Cynthia Brandt Stover

"It's a time of unparalleled innovation in health care, and Lucile Packard Children's Hospital Stanford has huge potential to improve the lives of children and families in the Bay Area and beyond," Brandt Stover said. "Philanthropy can unlock that potential. I'm honored to join the foundation and a dedicated team of doctors, donors, board members and staff. Together we will engage even more members of the community in this inspiring mission."

At the Smithsonian, Brandt Stover led the public phase of the institution's first-ever comprehensive fundraising campaign, which raised $1.88 billion, surpassing its $1.5 billion goal 16 months ahead of schedule.

Prior to joining the Smithsonian, she was vice president for institutional advancement at Mills College in Oakland, California, where she increased annual giving, tripled major gift solicitations and worked closely with the president and trustees on policy and organizational strategy.

"At Stanford Medicine, strategic relationships play a crucial role in our ability to lead the biomedical revolution in precision health, helping us to predict, prevent and cure the health conditions that impact the lives of countless children and families," said Lloyd Minor, MD, dean of the School of Medicine and a member of the search committee. "Cynthia has a track record of creating impactful relationships with institutional leaders, board members and colleagues, and her leadership will improve health outcomes not only in our local community but across the nation and world."

Brandt Stover is no stranger to Stanford. After receiving a bachelor's degree in English and fine arts from Vanderbilt University, she earned a master's degree and PhD in sociology from Stanford. She then served as associate dean for external relations at Stanford's School of Humanities and Sciences, where in 2008 her team surpassed the five-year fundraising average by 50 percent.

"We are grateful for the foundation's remarkable commitment to advancing children's health, which has helped Lucile Packard Children's Hospital Stanford grow and continues to help fund our transformational expansion," said Dennis Lund, MD, the hospital's interim CEO. "I look forward to working with Cynthia as she provides the leadership to ensure that more children and families receive the life-saving care they need."

Brandt Stover is the third president and CEO of the foundation, which was founded in 1997. She succeeds David Alexander, MD, who stepped down in March after holding the position for 11 years. **ISM**

OF NOTE

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

AISLING CHANEY, PhD, a postdoctoral scholar in molecular imaging, received a $65,000 grant from the Society of Nuclear Medicine and Molecular Imaging. The grant, funded by the Education and Research Foundation for Nuclear Medicine and Molecular Imaging, will support her work using PET imaging to study immune cells in the context of multiple sclerosis.

RONALD DALMAN, MD, the Dr. Walter C. Chidester Professor and professor and chief of vascular surgery, was elected vice president of the Society for Vascular Surgery for the 2018-19 academic year. In subsequent academic years, he will serve as president-elect and then president of the society.

NIRAJ DANGORIA, associate dean for facilities planning and management, received the 2018 Distinguished Service Award from the Society for College and University Planning, an organization of higher education leaders that works to develop individual and organizational planning capabilities. He was recognized for his long and diverse service to the society.

RONALD DAVIS, PhD, professor of biochemistry and of genetics and director of the Stanford Genome Technology Center, received a five-year, $3.7 million RO1 grant from the National Institutes of Allergy and Infectious Disease to the study the immunological basis of myalgic encephalopathy/chronic fatigue syndrome.

Aisling Chaney

SANJIV "SAM" GAMBHIR, MD, PhD, the Virginia and D.K. Ludwig Professor in Cancer Research and professor and chair of radiology, received the Benedict Cassen Prize for his pioneering work to bring together the fields of cell and molecular biology with biomedical imaging to form the field of molecular imaging, including the development of multimodality reporter gene technology. The $25,000 prize is awarded every other year by the Education and Research Foundation for Nuclear Medicine and Molecular Imaging to recognize work leading to a major advance in nuclear medicine science.

DEBRA KARHSON, PhD, a postdoctoral scholar in psychiatry, won second place in the Lasker Essay Contest from the Albert and Mary Lasker Foundation. The contest allows young scientists and clinicians to develop skills communicating important scientific issues to nonscientists. Her essay, "A verification vaccine for social contagion," proposes a method for authenticating the social media profiles of communicators to help users identify sources of accurate scientific information. The award includes $5,000.

JAYAKAR NAYAK, MD, PhD, was promoted to associate professor of otolaryngology-head and neck surgery, effective April 1. He specializes in the medical and surgical treatment of diseases of the nasal cavity and sinuses. His research focuses on restoring mucosal health following insult or inflammation using nasal stem cells; defining immune system abnormalities in chronic sinus diseases to improve therapies; and understanding and treating empty nose syndrome.

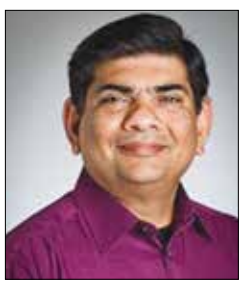
ANSUMAN SATPATHY, MD, PhD, instructor in pathology, received a 2018 Michelson Prize for Human Immunology and Vaccine Research. The $150,000 prize, established by the Human Vaccines Project and the Michelson Medical Research Foundation, supports young investigators who are working to develop future vaccines and therapies. His work combines genomics and human immunology to identify key gene regulatory mechanisms that trigger protective immunity following vaccination.

AUDREY SHAFER, MD, professor of anesthesiology, perioperative and pain medicine, was awarded the 2018 Ellis N. Cohen, MD, Achievement Award, the highest honor given to a faculty member by the Department of Anesthesiology, Perioperative and Pain Medicine. The award, named for the pioneering anesthesiologist whose research led to design changes for operating rooms, recognizes exceptional performance in teaching, research, clinical care or administration.

SHREYAS VASANAWALA, MD, PhD, was promoted to professor of radiology, effective May 1. His research focuses on developing methods to make MRIs quicker for children; quantifying cardiovascular and kidney function and assessing responses to cancer therapy using MRI; and designing and constructing improved MRI hardware. He is division chief of body MRI and director of MRI at Stanford Health Care and director of MRI at Stanford Children's Health.

HUMSA VENKATESH, PhD, postdoctoral scholar in neurology and neurological sciences, was named to the *MIT Technology Review*'s 2018 list of 35 Innovators Under 35. The list recognizes talented technologists whose work has the potential to transform the world. Her research has identified how tumor cells exploit neuronal signals to foster their growth, and she is working to develop innovative therapeutic approaches to impede that process. **ISM**

Ronald Dalman



Niraj Dangoria

Ronald Davis

Sanjiv "Sam" Gambhir

Debra Karhson

Jayakar Nayak

Ansuman Satpathy

Audrey Shafer

Shreyas Vasanawala

Humsa Venkatesh

Razina Aziz-Bose, Ritika Dutta named Howard Hughes Medical Institute medical research fellows

Two Stanford medical students, Razina Aziz-Bose and Ritika Dutta, have been named medical research fellows by the Howard Hughes Medical Institute.

The fellowship provides a grant of $43,000 to promising MD, DVM and DDS students so they can spend a year conducting biomedical research. Both Aziz-Bose and Dutta will conduct research at Stanford.

This year, 66 fellows were selected. They include Alyssa Flores, a student at the Geisel School of Medicine at Dartmouth, who will return to Stanford for the second year to investigate therapies for cardiovascular disease in the laboratory of Nicholas Leeper, MD, associate professor of surgery and of medicine.

In addition, Warren Chan of the Baylor College of Medicine; Corey Cheung of the UC-San Diego School of Medicine; Shaleeka Cornelius of the Meharry Medical College School of Medicine; and Lauren Platt of the UCLA David Geffen School of Medicine will pursue research projects at Stanford. **ISM**