Blood test for lung cancer tumors developed

By Jennie Dusheck

Profiling the genes of tumor cells from lung cancer patients' blood samples may be a cheap, noninvasive way to help doctors choose the right treatments, according to a study led by researchers at the School of Medicine.

The new findings strengthen the hope that evaluating the genetic profiles of tumor cells circulating in the bloodstream could transform cancer care: first, by indicating the next chemotherapy or targeted therapy to use when tumors evolve resistance to previous drugs; and, second, by providing a way to study how tumors change over time. The new blood test is safer, cheaper, faster and more effective than alternative diagnostic approaches, said the researchers.

The researchers created a system for isolating circulating tumor cells from the blood of cancer patients and reading a handful of genes from inside each tumor cell. Thus, they were able to obtain genetic information about the original cancer tumor that resides deep in the lungs without doing a biopsy, which can be dangerous for the patient.

"We are trying to make minimally invasive technology that allows us to continuously monitor one person's health over time," said radiology instructor Seung-min Park, lead author of the new study, which was published online Dec. 12 in the Proceedings of the National Academy of Sciences. Park shares lead authorship of the study with former Stanford graduate students Dawood Wong, PhD, and Chin Chun Ooi.

Tumor changes

It's common for cancer therapies to fail after a few months, often because the cancer evolves resistance to the treatment. At that point, it's important to understand how the patient's tumor is changing. "Without a biopsy and genetic profiling, we are flying blind, trying to select a second or third option for therapy and hoping it works," Wong said. But repeated lung biopsies are too hard on patients. Even CT scans, performed to see whether a tumor is shrinking or growing, increase management, including predicting response to therapy, will be much better optimized," Gambhir shares senior authorship of the study with Shan Wang, PhD, professor of materials science and engineering and of electrical engineering, and Viswan Nair, MD, clinical assistant professor of medicine and of radiology.

How it's done

The blood typically contains very few CTCs, so one of the challenges for oncologists has been to separate them from ordinary blood cells. The new technique involves taking blood from lung cancer patients and then attaching antibodies to circulating tumor cells. Once the cancer cells are labeled, the team introduces magnetic nanoparticles designed to attach to the antibodies labeling the cancer cells. With each individual cancer cell labeled with a magnetic nanoparticle, the researchers can then use a device called a magnetic sifter, or MagSifter, previously developed by Wang.

The MagSifter is an electromagnetic sieve that can be turned on and off. When the MagSifter is on, it pulls the nanoparticle-labeled circulating tumor cells from the blood of cancer patients.

Research locates absence epilepsy seizure ‘choke point’ in the brain

By Bruce Goldman

A particular structure in the brain is a "choke point" for a type of epileptic seizure that affects mostly children, School of Medicine investigators have found.

The researchers used an advanced technology called optogenetics to show, in rodent models of one of the most common forms of childhood epilepsy, that inducing synchronized, rhythmic activity in a specific nerve tract within this structure is sufficient to cause seizures, while disrupting that activity is sufficient to terminate them.

Epilepsy, a pattern of recurrent seizures, affects about 1 in 26 people over their lifetime, said John Huguenard, PhD, professor of neurology and neurological sciences and of molecular and cellular physiology. Absence, or petit-mal, seizures — a form of epilepsy most likely to occur among children ages 6-15 — account for about 1 in 20 cases of epilepsy. They are characterized by a sudden loss of consciousness, accompanied by a behavioral and postural freezing in place that typically persists less than 15 seconds. A child experiencing an absence seizure usually has no recollection of it.

"These seizures can be so subtle that they go unnoticed or are mistaken for a lack of attention," Huguenard said. The new findings, described in a study published in the journal Epilepsia, indicate that the most likely target for prevention is a "choke point" in the brain's control of electrical brain activity, which is known to arise in a specialized region of the brain called the thalamus.

Smartphones could be game-changing tool for cardiovascular research, study shows

By Tracie White

Widespread ownership of smartphones around the world could potentially transform cardiovascular research by providing rapid, large-scale and real-time measurement of individuals' physical activity, according to a new study by researchers at the School of Medicine.

"People check these devices 46 times a day," said Euan Ashley, DPhil, MRCP, associate professor of cardiovascular medicine. "From a cardiovascular health standpoint, we can use that personal attachment to measure physical activity, heart rate and more."

Ashley is senior author of the study, which was published Dec. 14 in JAMA Cardiology.

In March 2015, Stanford researchers launched a free iPhone app — MyHeart Counts — which gave users the ability to participate in a first-of-its-kind, easy-to-use cardiovascular research study. The app uses Apple's ResearchKit framework, which gives potential users a simple way to consent to participate, measure daily activities, complete tasks and answer surveys through their iPhone. Within six months of the app's launch, researchers had enrolled 47,109 participants from all 50 states who had consented to participate in the study.

Within weeks, researchers were able to collect data from 4,990 participants who completed a six-minute walk fitness test using the phone's built-in motion sensors — a number several times larger than the largest study previously published, the Co-Heart, page 4.

Within six months of its launch, the MyHeartCounts app had more than 47,000 users who had agreed to participate in a study tracking their heart health.
Tech support at medical school gets ‘lean,’ raises the bar for service

By Kris Newby

It’s 10 a.m. Monday, time for the lean team huddle at the Information Resources and Technology office on Porter Drive. On this day, team members review progress documenting the remote setup configurations of the hundreds of networked printers used at the medical school. It’s a daunting task, but posting this resource online will enable support staff to more rapidly connect new computers to printers and reduce the need to send field technicians out to customer sites.

This is just one example of how IRT support technicians are applying the “lean” approach, made famous by Toyota and other organizations, to improve customer value by engaging team members to recognize and solve problems.

Eight months after IRT’s first lean pilot project, results have been promising. Caller satisfaction is higher than ever, with 70 percent of survey respondents reporting positive experiences. And the average amount of time it takes for a caller to get a help-desk technician on the line is steady, improving, down from 112 to 24 seconds between August and November.

In addition to revamping its processes, the IRT group has upgraded its infrastructure and launched new customer-focused services. They’ve installed a state-of-the-art call system that displays help requests and wait times on large monitors around the office. When callers wait too long, their listings turn red, signaling help-desk technicians who are working on requests that aren’t time-critical to lend a hand. They’ve also opened a walk-in tech support bar in the basement of Lane Medical Library, complete with loaner computers for employees whose own machines are being repaired.

Looking back over the last year, Jesse Mena, an IRT service technician and a lean team member, said, “There’s been a revolutionary change in our approach to customer service.”

The lean launch

Last March, the IRT group formed its first lean team to improve the efficiency in the help-ticket process. The project started with a three-day launch, attended by representatives from the help-ticket team and a lean consultant.

In the first phase, participants documented each step of the help-ticket process by posting sticky notes along a wall. At the end of the day, the team was surprised at the complexity of the workflow, illustrated with 15 feet of branching and looping sticky notes. The flaws in the process were laid bare, revealing that some help tickets had the potential to get stuck in the system for up to 40 days.

Next, the team learned how to integrate the lean process into the IRT work environment to improvearanage system with a good idea could write it on a sticky note and post it to a visualization board in the tech support area. During Monday huddles, ideas are discussed by all the team members, keeping in mind the lean mantra: “How can we quickly learn what ideas work, then discard the ones that don’t?” If the group decides that an idea has merit, it is systematically moved through planning, testing and deployment phases. The weekly huddles create a mechanism that keeps subprojects moving and prevents good ideas from getting stuck in the cracks.

A bottom-up approach to problem-solving

Amber Burleigh, a service desk technician, said she likes the way the lean process is slowly changing the way the organization identifies and fixes problems.

“My job involves problem-solving on a daily basis. I was looking for ways to improve my process, so I thought about trying the lean approach. The first step was to identify a small problem and start working on it. Then I moved on to bigger and better ideas.”

The team’s director, Bonnie Tsang, previously led lean improvement efforts at Lucile Packard Children’s Hospital Stanford, and is eager to assist other interested groups.

She acknowledged that there are unique challenges to establishing lean practices in academic settings. These institutions typically have complex organizational and decision-making structures and frequently need to balance multiple missions, she said.

Tsang is a soft-spoken, thoughtful evangelist for lean. Her job entails educating employees about lean, helping teams embrace change and motivating them to continuously improve. She adds, “Our motto is to empower innovation by every person every day.”

To learn more, go to https://med.stanford.edu/financials/process-excellence.html

Lora Purtle of Information Resources & Technology walks by a visualization board that tracks the progression of ideas for improving services.

Could eating caviar be a ‘risk factor’ for having lots of money?

By Krista Conger

It was an hours-delayed flight and a $10 food voucher that did it. Annoyed, Anders Huitfeldt, PhD, a postdoctoral scholar at the Meta-Research Innovation Center at Stanford, or METRICS, decided to spend his voucher on the most impractical item he could find in the airport. After some searching, he found it: a minus-cule spoon of high-end caviar.

“It was the smallest amount you could possibly have,” he said. “And it was wonderful, I kind of got addicted.”

The experience got Huitfeldt thinking, but not just about fancy caviar. As a researcher at METRICS, he is interested in making scientific research findings more accurate and reproducible. “I have had a long-standing interest in trying to understand why published research papers often fail to find the truth,” he said.

“It seems that often researchers are confused about what they are actually trying to do.”

Huitfeldt explored that problem in the British Medical Journal’s Christmas issue—a light-hearted collection of articles that address important scientific concepts. His piece, “Is caviar a risk factor for being a millionaire?” examines how the term “risk factor” can have at least four distinct meanings in scientific literature. For example, does caviar consumption predict current wealth (i.e., is diagnostically helpful) or the likelihood of amassing wealth in the future (is prognostic)? Does it actually play a role in how wealth accumulates? (For example, does eating the fish eggs make you a stock-market investor?) Or does the act of caviar consumption simply increase the probability of wealth, perhaps by bringing the consumer into close proximity of other wealthy movers and shakers with whom profitable deals can be struck? The outcome of the study varies tremendously depending on what the researchers mean by ‘risk factor,’ Huitfeldt said. “Until they agree, it’s not even clear how the question should be addressed. And this uncertainty becomes a serious impediment to processing information correctly to make the best decisions.”

For a more in-depth look at the many issues affecting research reproducibility, and the ways that Stanford scientists are attempting to address them, check out “Can you repeat that?” in the summer 2016 issue of Stanford Medicine magazine.
Some glioblastoma patients benefit from ‘ineffective’ treatment

By Krista Conger

A subgroup of patients with a devastating brain tumor called glioblastoma multiforme benefited from ‘ineffective’ treatment with a class of chemotherapy drugs that two previous large clinical trials indicated was ineffective, according to a study at the School of Medicine.

Specifically, patients in the subgroup who were treated with chemotherapy drugs that block the growth of new blood vessels in the tumor lived an average of about one year longer than those who were given other classes of chemotherapy drugs, the researchers found.

The retrospective study emphasizes the importance of properly categorizing tumors with varied biology in order to best personalize treatment for each patient. Lumping all glioblastoma patients together as one group led to the flawed conclusion that no patients benefited from anti-angiogenesis treatments, the researchers said.

“Traditionally, glioblastoma patients are given this diagnosis based on the histology of their tumor, and then assigned a grade and a stage,” said Daniel Rubin, MD, associate professor of biomedical sciences and of radiology and of medicine. “But this information is not always specific enough to clearly inform treatment. We’ve developed a new method of classifying glioblastomas by quantitatively analyzing the magnetic resonance imaging that is routinely performed during diagnosis.”

Rubin is the senior author of the study, which was published online Dec. 22 in Neuro-Oncology. Postdoctoral scholar Tiffany Ting Liu, PhD, is the lead author of the paper.

A deadly brain tumor

Glioblastoma multiforme, also known simply as glioblastoma, is one of the most common, and most deadly, brain tumors. About 12,000 people in the United States are diagnosed each year with the disease. The median survival is about 15 months after diagnosis. Until recently, clinicians and patients pinned their hopes on a class of chemotherapy drugs called anti-angiogenic compounds that are meant to block the growth of new blood vessels into the tumor. Blocking this growth, it was believed, should starve the tumors of oxygen and nutrients. However, two large, phase 3 clinical trials recently reported in The New England Journal of Medicine concluded that one such drug, bevacizumab, conferred no survival benefit on glioblastoma patients.

Liu, Rubin and their colleagues wondered if there might be a subgroup of glioblastoma patients that could still be helped by the treatment. They studied the medical records and diagnostic images of 69 glioblastoma patients who had been treated at a local medical center and 48 patients from a national database known as The Cancer Genome Atlas.

“The researchers used specialized software to categorize each patient into one of two groups based on the degree of vascularization of the patients’ brain tumors. Those whose tumors were more highly vascularized — as determined by an imaging technique called perfusion MRI — were significantly more likely to benefit from treatment with anti-angiogenic therapies than those whose tumors were less well vascularized.”

Differences in glioblastoma biology

Perfusion MRIs are routinely conducted as part of the diagnostic procedure for brain tumor patients. The researchers found that each of the 117 patients fell neatly into one of two clusters: 51 of the patients had tumors that were highly vascularized, and 66 had tumors that were not as well vascularized. Further investigation showed that the highly vascularized tumors also expressed more genes involved in blood vessel growth and in protecting cells from conditions of low oxygen called hypoxia than tumors of patients in the other group. Rubin and his colleagues then looked to see what treatments the individual patients had received, and how they fared.

“The most exciting finding was that those members in the highly vascularized group who had received anti-angiogenic therapy lived significantly longer — on average more than a year more — than those in the same group who did not get anti-angiogenic therapy,” said Rubin. “And this analysis was performed using images that already exist as part of the diagnostic procedure for this disease. Our findings speak to the fact that the biology of glioblastoma can vary significantly among individuals, and that certain subgroups of patients may benefit from treatments that appear ineffective for others.”

Rubin and his colleagues hope their study will reignite the conversation about the use of anti-angiogenic therapies in glioblastoma, while also enhancing the understanding of the varied biology of the disease.

“This is a turning point,” said Rubin. “We believe we can identify those people who are likely to benefit from anti-angiogenic treatments, and also begin to think outside the box to identify other types of therapies for those who are unlikely to respond. This shows that subtyping can dramatically change our understanding of the disease and how we treat it.”

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.

Other Stanford co-authors are adjunct clinical instructor Lex Mitchell, MD; former medical student Scott Rodriguez, MD; medical student Abigail Ferrero; clinical assistant professor of radiology Michael IV, MD; clinical instructor of radiology Christine Kim, MD; clinical assistant professor of neurosurgery Navjot Chaudhary, MD; assistant professor of medicine and of biomedical data sciences Olivier Gervais, PhD; professor of neurosurgery Griffith Harsh, MD; and professor of neurosurgery Steven Chang, MD.

The research was supported by the National Institutes of Health. Stanford’s departments of Biomedical Data Science, of Radiology and of Medicine also supported the work.

$26.4 million awarded to researchers for physical activity study

By Tracie White

Stanford researchers have been awarded two grants totaling $26.4 million as part of the largest program ever funded by the National Institutes of Health to study the biological mechanisms of physical activity.

Michael Snyder, MD, professor and chair of genetics, and Stephen Montgomery, PhD, assistant professor of medicine and of genetics, were awarded $15.7 million. They will lead a research team using advanced technological tools to identify and characterize the entire range of molecules that form during or after exercise.

“Our grant is to collect genomic, transcriptomic and epigenomic information and learn about how these relate to the effect of exercise,” Snyder said. “We will be determining how exercise affects the body’s biochemistry at a detailed level never analyzed previously.”

Montgomery added, “A lack of physical activity is a major factor in multiple diseases. This program provides an exciting opportunity to learn the molecular mechanisms underlying physical activity, with the goal of enabling new approaches to improving or maintaining individual health.”

A bioinformatics center

A second grant of $10.7 million was awarded to Euan Ashley, DPhil, MRCGP, associate professor of cardiovascular medicine and of genetics, to establish and lead a bioinformatics center for data storage and access available to all the researchers across the NIH program.

“The role of the bioinformatics center will be data integration in collaboration with other datasets, and novel analytics,” Ashley said.

The NIH program, called Molecular Transducers of Physical Activity in Humans, will award a total of $170 million to researchers across the United States over the next six years to study the molecular changes that occur during and after exercise, with the goal of advancing the understanding of how physical activity improves and preserves health.

“The development of a so-called molecular map of circulating signals produced by physical activity will allow us to discover, at a fundamental level, how physical activity affects our health,” Francis Collins, MD, PhD, director of the NIH, said in a news release. “The study will help us understand how exercise affects our health, and whether or not it is beneficial.”

The program will include seven clinical trial sites across the country and seven chemical analysis sites. Three awards will go to conduct physical activity studies in animal models. The bioinformatics center will disseminate data and tools to the entire research community, and a coordination center will facilitate activities across the consortium.

“What is so exciting about this program is that there is no more potent therapeutic intervention than exercise,” Ashley said. “Although exercise reduces the risk of almost every disease you can think of — heart disease, lung disease, cancer, neurological disease, GI disease, bone disease, back pain, depression and so on — and yet, we have no tool that exercises achieves this magical effect.”
Accuracy vs. estimates

Researchers have already established the importance of physical activity, fitness, sleep and diet in maintaining cardiovascular health, the study noted. Low fitness levels, in particular, are a key risk factor for heart disease, with previous research indicating that insufficient physical activity accounts for 5.3 million deaths per year worldwide. But in most of the prior clinical studies, researchers have relied on participants to estimate the time spent on physical activity. And people have been consistently shown to overestimate their activity levels, the study noted.

"Traditional research on physical activity and cardiovascular health has been based on people writing down what they remembered doing," McConnell said. "Mobile devices let us measure more directly people's activity patterns through activity data with researchers. The upgrades include the research app that allows willing participants to share heart health and behavior data with researchers. The upgrades include the Stanford Coaching Module, which will test a series of four health interventions — prompts and suggestions aimed at improving heart health; more user feedback; graphs showing how a user compares to others in terms of steps taken each day, amount of sleep and happiness.

Stanford Coaching Module

"I'm excited to be able to deliver more data back to the patient," said Euan Ashley, DPhil, MB, MRCP, an associate professor of cardiovascular medicine and of genetics at Stanford and the principal investigator on the MyHeart Counts team. "We collect a lot of personal information from participants in the hope that we can improve methods of preventing heart disease."

Researchers are working on an Android version of the MyHeart Counts app to broaden the reach of the ongoing study, as well as an updated version of the app that will include more motivational feedback to the users about how to improve their heart health.

"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," said McConnell. "Other Stanford authors are Alek San- dra Pavlovic, MyHeart Counts project manager; graduate students Julian Homburger and Rachel Goldfeder; Daryl Waggott, bioinformatics statistician; Mildred Cho, PhD, professor of pediatrics; Mary Rosenberger, PhD, cancer scientist; William Haskell, PhD, professor emeritus of medicine; Jona than Myers, PhD, clinical professor of medicine; Mary Ann Champagne, clinical nurse specialist; Emmanuel Mignot, MD, PhD, professor of psychiatry and behavioral sciences; Robert Harrington, MD, professor and chair of medicine; and Alan Yeung, MD, professor of cardiovascular medicine."

The researchers received software development support from Apple Inc. Stanford's Department of Medicine also supported the work.

Coaching module among upgrades to MyHeart Counts app

By Jennie Dusheck

Resolved to improve your heart health in the new year? A newly updated app could keep you on track.

Researchers at the School of Medicine have launched MyHeart Counts 2.0, a major update to the popular research app that allows users to share heart health and activity data with researchers. The upgrades include the Stanford Coaching Module, which will test a series of four health interventions — prompts and suggestions aimed at improving heart health; more user feedback; graphs showing how a user compares to others in terms of steps taken each day, amount of sleep and happiness.

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The researchers received software development support from Apple Inc. Stanford's Department of Medicine also supported the work.

Wall Street Journal
Gene activity predicts progression of autoimmune disease

By Jennie Dusheck

Researchers at the School of Medicine and six other institutions have designed a new diagnostic tool for a rare and deadly autoimmune disease that affects the skin and internal organs.

By measuring the activity of genes in tiny skin samples, the researchers were able to predict disease progression in patients as much as a year earlier than clinicians, who use standard measures.

The study was published Dec. 22 in JCI Insight. The lead authors are Shane Logfren, a research associate at Stanford, and Monique Hinchcliff, MD, associate professor of medicine at Northwestern University. The senior author is Purvesh Khatri, PhD, assistant professor of medicine at Stanford.

Systemic sclerosis, also called scleroderma, is an autoimmune disease that causes scarlike thickening of the skin and internal organs, such as the kidneys and lungs. According to Hinchcliff, systemic sclerosis affects about 100,000 people in the United States.

A better test

The cause of systemic sclerosis is unknown, and there are no drugs approved by the Food and Drug Administration for treating it. Many patients are given drugs that are approved for use in other diseases, but each drug is clinically effective in only a fraction of patients.

To find out if a patient is responding to treatment, clinicians use a test called the modified Rodnan skin score, in which a doctor pinches the skin to see how thick it is. For the test, the physician squeezes the patient’s skin in 17 places, rating the thickness of each pinch of skin on a scale of 0 to 3 and adding the scores together for a maximum score of 51.

“It’s a very subjective measure,” Khatri said. He noted that despite careful training, doctors may give the same patient different scores, depending, for example, on the patient’s body mass index.

Different physicians evaluating the same patients may agree only 60 to 70 percent of the time, Hinchcliff said. “It’s difficult to produce a disease management team in which a doctor pinches the skin to see how much it thins,” he said, “while all the data for the scleroderma patients fall within another.”

Getting results a year earlier

The team looked at data from a cohort of Northwestern University patients who had been tested repeatedly with the skin pinch test while being treated with a drug. The 45 test — applied to this preexisting set of patient data — could distinguish patients who were improving from those who were not 12 months after their treatment began.

In contrast, the doctors’ skin pinch test from the same set of data took 24 months to identify which patients were improving.

“In the data from Northwestern, all the patients were getting exactly the same treatment, the same drug,” said Khatri. “Yet we were able to predict a year before the clinician which patients were getting better and which were getting worse.”

Clinical trials, as opposed to retrospective studies looking at pre-existing data, are needed to validate the 45 test, the researchers said. But if it works as well as Khatri and his collaborators hope, clinicians may be able to evaluate patients’ response to treatments much more quickly, so they can be switched to some other treatment that may work. The test could also help advance the search for better therapies.

“What was really cool was that we could predict on an individual level which patients would get better or worse,” said Khatri.

Scleroderma is an autoimmune disease that causes scarlike thickening of the skin and internal organs. It can cause skin lesions like those pictured above.

“Getting results a year earlier could distinguish patients who were improving from those who were not 12 months after their treatment began.”

So, he added, his team will begin giving EGFR-inhibiting drugs to mice with a sclerodermalike condition to see if it helps.

“It’s very exciting,” said Khatri. “This is a disease that has stumped people for more than 25 years.”

Other Stanford co-authors are professors of dermatology David Fiorentino, MD, PhD; professor of medicine Paul Utz, MD; associate professor of medicine Lorinda Chuang, MD; postdoctoral scholars Peggie Cheung, PhD, and Alex Kuo, PhD; and rheumatology fellow Antonio Valenzuela, MD.

In addition to Northwestern, researchers at the following institutions also contributed to the study: Dartmouth College, the University of California-San Francisco, the Hospita1 for Special Surgery, the University of Texas Health Science Center and the Veterans Affairs Palo Alto Health Care System.

The research was supported by the National Institutes of Health, the Bill and Melinda Gates Foundation and the Scleroderma Research Foundation.

The Stanford Department of Medicine also supported the work.

Starfish larvae create complex water whorls to eat and run

By Tom Abate

Peek into a tide pool and you may see a starfish clinging firmly to a rock. But its secure adulthood comes at the expense of a harrowing larval journey.

Tiny starfish larvae — each smaller than a grain of rice — spend 60 days and 60 nights paddling the open ocean, feeding to accumulate the energy needed to metamorphose into the familiar star shape.

Now, a team of Stanford scientists has revealed the beautiful and efficient mechanism that allows these humble creatures to survive to adulthood.

The findings are described in a paper published Dec. 19 in Nature Physics. Manu Prakash, PhD, assistant professor of bioengineering, is the senior author. The lead author is graduate student William Gilpin.

“Starfish have shown that nature equips these larvae to stir the water in such a way as to create vortices that serve two evolutionary purposes: moving the organisms while simultaneously bringing food close enough to grab,” Prakash said. Using experimental techniques that capture the visual beauty and mathematical underpinnings of this mechanism, the researchers show how the shape and form of starfish larvae enable the functions that are necessary to support life.

When we see strange and beautiful shapes in nature we bring them back to the lab and ask why they evolved this way,” Prakash said. “That is the perspective we bring to biology: to understand mathematically how physics shapes life.”

Gilpin said these findings shed light on similar evolutionary challenges involving diverse organisms that are related to starfish larvae in a key way.

“Evolution seeks to satisfy basic constraints,” Gilpin said. “The first solution that works very often wins.”

These experiments began in the summer of 2017 when Prakash’s colleague in Pacific Grove, California, the researchers were taking a course on embryo1ogy when they began to wonder about the evolutionary origins of the starfish larva’s shape. Why did it end up looking as it did? Bringing their background back to the Prakash lab, the group started toying with systems in a systematic way, feeding the larvae nutrient algae and observing their movements with video-enabled microscopes.

Our first eureka moment came when we saw the complex vortices
Cancer
continued from page 1

The technique serves as a proof of concept for collecting and analyzing lung cancer cells from blood samples. If the technique receives approval from the Food and Drug Administration, it could be used to tell how cancer cells have evolved in response to chemotherapy, which drug is the best to use next in individual patients.

In principle, the technique should work just as well with cancers in other organs, “We validated our device on lung cancer because of the difficulties of doing lung biopsies,” he said. “But the technology is not limited to profiling lung cancer. We believe that other cancers are in the offing, too.”

Epilepsy
continued from page 1

online Dec. 15 in Neuron, point to the spreading influence of ways of reducing, halting or possibly even preventing absence seizures. If successful, “that would be a game changer,” said Paz. “It took a lot of reasoning to think these findings may also apply to a wider range of generalized seizure types, including the more severe types where children have an abnormal gait, are characterized by involuntary jerking movements in addition to loss of consciousness.”

Huguenard shares senior authorship of the study with Jeanne Paz, PhD, a former postdoctoral scholar in his group and now assistant professor of neurology at the University of California-San Francisco and assistant investigator at the Gladstone Institutes in San Francisco. After Paz, who initiated the study, departed for UCSF, the experiments were continued by Stanford graduate student Jordan Sorokin, the study’s lead author, under Huguenard’s direction.

Multiple daily seizures

“Many people think of absence seizures as being mild because there’s no shaking or falling on the floor,” said Paz. “But some kids have more than 200 absence seizures a day, making it impossible for children to go to school. And the drugs they take for their seizures may not work well.”

Absence seizures are a type of so-called generalized seizures: patterns of rhythmic nerve-cell firing activity that, while originating in one or another brain region, propagate throughout the entire organism.

Implicated in all generalized seizures is a nerve circuitry in a deep-brain structure called the thalamus, whose functions include relaying sensory information to the cerebral cortex via a nerve projection called the thalamocortical tract.

Resorting to an increasingly widely used approach called optogenetics pioneered in the lab of study co-author Karl Deisseroth, MD, PhD, a Stanford professor of bioengineering and of psychiatry and behavioral sciences, the researchers inserted the gene for a light-sensitive cell-surface protein called an opsin into a set of excitatory nerve cells in the thalamocortical tract of rats and mice bred to be prone to absence seizures.

As a result of this manipulation, the opsins appeared on the surfaces of those excitatory nerve cells, and the particular opsins the scientists used for some of their experiments was inhibitory. In essence, its presence on nerve cells meant that whenever yellow light was delivered to them via an implanted fiber-optic cable, those cells would be prevented from firing.

The thalamocortical tract’s excitatory nerve cells are somewhat like excitable muscles. Imagine a cake filled with children who share an inability to stay completely quiet for more than a few seconds. Imagine, further, a teacher who does not find the occasional loud whisper or random outburst but who will not abide noise above a certain threshold. When the din exceeds a critical level, the teacher shouts a show-stopping, “Quiet!”

The inevitable result of this enforced silence: Five seconds later, the room will erupt in a burst of noise, in turn inducing an authoritarian cease-and-desist command, followed by another eruption, and so forth. The very act of inhibiting behavior often triggers a pattern of rhythmic firing.

Disrupting the pattern

Similarly, back in the thalamus, inhibition (the “teacher” analog) is meted out to the thalamocortical tract’s excitatory nerve cells by a different set of cells in the brain known as thalamocytes that are capable of guiding excitatory thalamocortical nerve cells from a tightly synchronized to a more chaotic firing pattern may be able to halt absence seizures — and, maybe, other forms of generalized epilepsy, too.

Other Stanford co-authors of the study include Schönheider, Prakash, Mehran Jamali, MD; clinical research associate Carissa Toggood; and Mehran Jamali, MD, PhD.

The work was supported by the U.S. Army Research Laboratory’s Multidisciplinary University Research Initiative for the Environment.

The financial support of the U.S. Army Research Laboratory’s Multidisciplinary University Research Initiative for the Environment.

As they considered the implications of these findings, the researchers hypothesized that this feed-versus-speed mechanism likely applied to other invertebrate larvae that, though different than starfish larvae in form, are nonetheless known to have similar ciliary bands. In future experiments, the researchers plan to use the same techniques to study other larval shapes. What they hope to learn is how evolution has taken a certain mechanism — larval anism, the ciliary band, and solved the same feed-versus-speed trade-off in dozens of different forms of life.”

“Starfish conformed from page 5

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The research in Epilepsy.

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The research in Epilepsy.
**Making bread is an art, science and passion project for Fiona Strouts, PhD, a research scientist in infectious diseases at the School of Medicine. Her baking began as a hobby several years ago, but now Strouts operates a business, L’atelier du Pain, and sells her whole-grain bread at the Portola Valley Farmers Market. Recently, Jennifer Huber, a frequent contributor to the school’s blog, Scoop, caught up with her by email.**

1 How did you start baking bread? **STROUTS:** I learned to make bread about eight years ago from my Italian housemate when I lived in London. I’m told that many of my colleagues thought to make 100 percent whole-wheat sourdough bread that we would bake together on the weekends. The bread was fairly dense, and provided good fuel for cycling. I also learned to make whole-grain, naturally leavened breads using mostly California-grown wheat. The favorite seems to be the Sproused Lentil & Rye bread. But my personal favorite is the Sonoma Field Blend; it has great flavor and aroma. Sonora wheat was one of the first varieties planted in California in the early 1800s.

2 I’ve heard that you grind your own wheat. Why? **STROUTS:** Yes, I stone-grind my own wheat because I want to capture the flavor and nutrients, which come mostly from the germ and bran portions of the wheat berry. I buy bags of wheat berries directly from the mill and mill them into flour right before I mix the dough. Milling the wheat myself also ensures that the flour is 100 percent whole grain. Wheat is very numerous in California, and there are more than 20 different varieties that make it easier or harder for farmers to produce, depending on the conditions. I also wanted to recreate something similar to the way in which I was raised. It reminds me of my family and the Czech Republic, which is a specialty that attracts an interest in health. And whether we’re able to detect the presence of bacteria in the blood of healthy people, to help investigators what we see in sick individuals with suspected infections. My background has helped me understand sustainable agriculture and who are growing different types of wheat.

3 Why did you decide to turn your hobby into a business? **STROUTS:** A number of things inspired me, and they all came together a few months ago. I grew up in France, and in the village where my parents lived there was a family of bakers who had been baking bread for years. I was going to the market on Saturday, and after stopping by his house to pick up bread, there would be others from the village there, and I would save a sample and a glass of wine before picking up the bread and going home for lunch. I miss that sense of community, and I wanted to recreate something similar.

4 Then about a year ago, I started learning more about the different, often unique, combinations of sustainable agriculture and who are growing different types of wheat. I was eventually in the process of changing direction and turned to the school for help. Changing direction can be a difficult and long journey. How do you juggle baking, running a business and doing research? **STROUTS:** Good question! It takes organization and prioritization. I used to bike to race, and the training required a lot of discipline. But starting the business was less structured, and it took longer than I thought it would, as I was doing it in my spare time. I spent several weekends practicing baking large batches of bread and sharing it with some of my labmates, which I think they appreciated. The market is one day per week, and it’s a manageable scale for one person. I’ve reduced my full-time equivalent [work] hours accordingly very supportive.

5 Explain your research at Stanford. Has it given you any insights into bread-making? **STROUTS:** I work in the lab of David Relman, MD, on a project focused on improving the diagnosis and treatment of systemic infections in humans, understanding quenching of both microbial nucleic acids and host transcripts derived from blood. I am trying to understand what those profiles look like during states of health and disease. And whether we’re going to detect the presence of bacteria in the blood of healthy people, to help investigators what we see in sick individuals with suspected infections.

By Kristy Crawford

Fiona Strouts began baking bread as a hobby several years ago, but now she operates a business, L’atelier du Pain, and sells her whole-grain bread at the Portola Valley Farmers Market.
Therapy dogs take a bite out of student stress before exams

By Kris Newby
Erin Devine, PhD, a first-year medical student at the School of Medi-
cine, was on her way to study for an anatomy final when she was stopped in her tracks by a pack of dogs.

The animals immediately went to work, dissipating the worries of Devine and other students by making themselves available for hugs and of-
fering up free kisses. Therapy dogs, it seems, enjoy their jobs.

“I’ve always loved playing with dogs. Their affection and kisses are a great way to de-stress and take your mind off studying for a few minutes,” said Devine, as she scratched one of the dogs’ necks. The dog, Crosby, licked her face in gratitude.

Beyond the anecdotal reports that say loving dogs make people happy, there’s a growing body of evidence that visiting therapy dogs promote emotional and physical health among students. This year, a randomized study out of Virginia Commonwealth University suggested that col-
lege-aged students felt significantly less stress after interacting with ther-
apy dogs for just 15 minutes. And for many of the students, this experience brings back happy memories of be-
loved family dogs.

Margaret Goves, director of medi-
cal student wellness, is an enthusiastic supporter of Stanford’s therapy dog program, and she works with Mar-
tha Kessler, leader of the comfort dog pack, to schedule therapy sessions throughout the year.

Therapy dogs take exams, too, said Kessler, who is also an execu-
tive director of finance and admin-
istration at the School of Medicine. Her 6-year-old golden retriever, Oli-
ver, undergoes training and testing throughout the year. So far he has passed tests for canine good citizen advanced, beginning novice odi-
dence, companion dog and therapy dog certifications.

She thinks the best therapy dogs are born with heightened qualities of empathy and calmness. Oliver, for example, is part of an accomplished line of comfort dogs: His mother provides Wesleyan students with therapy, his sister visits Yale students during exams and his brother regu-
larly holds sessions at the University of Massachusetts.

After the student therapy session was over, Oliver and Kessler went to the third floor of the Li Ka Shing Center for a short visit with Lloyd Minor, MD, who is a pet parent of two Portuguese water dogs, as well as the dean of the School of Medicine.

“Even medical school deans can benefit from comfort dog therapy,” said Kessler.

State stem cell agency awards Strober $6.6 million

Samuel Strober, MD, a professor of medicine, was awarded $6.6 million by the governing board of the Cali-
ifornia Institute for Regenera-
tive Medicine on Dec. 15 to conduct a phase-1 clinical trial to test a new way of inhibiting the rejection of transplanted kidneys. The award marked the 10th clinical trial funded by the institute in 2016.

The clinical trial will test whether injecting blood stem cells and T cells from the kidney donor at the time of transplant will enable the recipient to more readily ac-
cept the new organ. The institute called the approach, which would hopefully eliminate the need for ongo-
ing immunosuppressive drug treatment, “deceptively simple” in a blog post about the awards.

About 17,000 kidney transplants are performed in the United States each year. Recipients must undergo a lifetime of anti-rejection drugs, which increase their risks of infection, cancer and heart disease.

Strober’s award was one of two approved at the meeting. An additional $8.3 million was awarded to University of California researcher Henry Klassen, MD, PhD, and the biotech company JCyte to continue clinical trials on a treatment for retinitis pigmentosa, a progressive, inherited eye disease that causes blindness in early adulthood.

Please give blood

Blood type needed: O-

To request an appointment, call 723-7831 or you can make an appointment online.

3323 Hilview Ave., Palo Alto
445 Burgess Drive, Menlo Park
435 South Dr. Mountain View
http://bloodcenter.stanford.edu

Stem cell therapy dogs help medical student Erin Devine de-stress on her way to study for a final exam.

Sui Wang
Katja Weinacht
J. Bradley Zuchero

Thomas Robinson
Prasanna Jagannathan
Maximilian Deihm

Lagrimadora Bintu, PhD, was appointed assistant professor of bioengineering, effective Jan. 1. Her research focuses on understanding the dynam-
ics of gene and chromatin regulation to improve mammalian cell engineering.

Thomas Cherpes, DVM, MD, was appointed assistant professor of comparative medicine, effec-
tive Dec. 1. His research interests include the ef-
fect of female hormones on immune responses to genital-tract pathogens, host responses to chlamydia infection and the development of cellular immuno-
therapy for cancer.

Maximilian Deihm, MD, PhD, assistant professor of radiation oncology, was elected to the American Society for Clinical Investigation. He was recog-
nized for his work focusing on genetic immune diseases and immune dysregulation. His research examines the relationship between mitochondrial bioener-
genetics and cell development and explores the use of stem cell therapy for patients with DiGeorge syndrome.

J. Bradley Zuchero, PhD, was appointed as-
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