Unroofing relieves symptoms of heart anomaly

By Tracie White

In 2010, Ingela Schnittger, MD, a cardiologist at the School of Medicine, sat in her lab examining the echocardiogram of a young man who came to the heart clinic at Stanford Health Care complaining of chest pain. She spotted a curious motion of the heart on the computer screen, one that she’d seen before while examining these kinds of diagnostic tests.

“All of the sudden I had this flash-back,” she said. She remembered a young physics professor at another institution who had suddenly dropped dead of a heart attack while running on a treadmill. During an autopsy, a little-known heart anomaly called a myocardial bridge was found. The term describes a condition in which a major artery runs through the muscle of the heart rather than resting on top of the organ.

“I was thinking, ‘Wow, I wonder if this patient could have a myocardial bridge?’” she said. Six years later, Schnittger, professor of cardiovascular medicine, has co-authored four research studies on myocardial bridges. A fifth, published online Oct. 13 in the Annals of Thoracic Surgery, finds that a procedure called surgical unroofing is safe and provides surgical unroofing to many patients with incapacitating symptoms, such as chest pain, arrhythmias and fatigue, that are not helped by medication alone.

Schnittger is senior author of the study, and the lead author is Jack Boyd, MD, clinical assistant professor of cardiothoracic surgery.

Myocardial bridging remains a mystery to much of the medical community. “It’s a congenital anomaly that was discovered during autopsies almost 300 years ago, but it has long been considered benign, the study said. Bridging continues to be little understood and is often misdiagnosed, Boyd said. “It’s not taught in medical school, and there is no agreed-upon treatment,” he said.

That lack of understanding about the condition is what sent Schnittger along her path of investigation. She wanted to know more: Could bridging be dangerous? Did it cause symptoms? How should it be treated?

In 2011, Schnittger designed a study at Stanford to enroll patients with undiagnosed myocardial bridging to much of the medical community.

Stanford Medicine, VA will collaborate to build nation’s first hadron therapy center

By Krista Conger

Many cancer patients are familiar with radiation therapy, in which beams of electrons are used to kill cancer cells. But photon beams can also adversely affect neighboring normal tissue. This toxicity limits both the dose that can be delivered and the size of the tumor that can be treated effectively.

Now, Stanford Medicine and the Veterans Affairs Palo Alto Health Care System have announced a collaboration to establish the nation's first center to deliver hadron therapy to cancer patients. Hadron therapy — which relies on beams of charged particles like protons, carbon, helium and other ions — is expected to increase cancer cure rates because it can treat multiple tumors or those resistant to conventional radiotherapy, while also limiting adverse side effects.

“Through our precision health vision, Stanford Medicine is committed to providing more personalized health care that is tailored to each individual,” said Lloyd Minor, MD, dean of the School of Medicine. “Planning for the hadron center embodies this commitment, as we seek to identify optimal ways to offer targeted treatment that both reduces harm and promotes healing.”

Killing tumors with charged particles

The collaboration was announced at an event Oct. 17 at the White House as part of Vice President Joseph Biden’s Cancer Moonshot initiative. At the event, the vice president shared the Moonshot Committee's report.

Hadron therapy uses beams of charged particles like protons, carbon ions and other ions to kill tumor tissue.

Researchers predict with high accuracy if antidepressants will help

By Tracie White

Using brain scans combined with a personal history of any early life trauma, such as abuse or neglect, researchers at the School of Medicine successfully predicted with 80 percent accuracy whether antidepressants would help patients recover from depression.

“We think our results are especially strong because we demonstrated that accuracy is robust by confirming it with cross-validation techniques,” said Leanne Williams, PhD, professor of psychiatry and behavioral sciences.

A paper describing the findings was published online Oct. 17 in the Proceedings of the National Academies of Science. Williams is the senior author. Postdoctoral scholar Andrea Goldstein-Piekarski, PhD, is the lead author.
Three individuals to receive medical school's highest honor

By Ruthann Richter

A distinguished physician-scientist, a lawyer with a long record of public service and a Silicon Valley entrepreneur and philanthropist are this year's recipients of the Dean's Medal, the highest honor bestowed by the School of Medicine.

The 2016 medal recipients are Ann Arvin, MD, the Lucile Salter Professor of Pediatrics and the university's vice provost and dean of research; attorney John Levin, chair of the Stanford Health Care board of directors; and entrepreneur and philanthropist Sean Parker.

"The awards honor individuals who have made scientific, medical, humanitarian, public service or other contributions that have significantly advanced the mission of the School. The medals will be awarded today at a ceremony."

"This year's medal recipients have dedicated their lives during the past century to the extraordinary opportunities I've had over these many years. I don't feel I should be honored for. I feel quite the opposite."

"I'd like to thank Dean Minor and the entire team at Stanford Medicine for this extraordinary recognition," Parker said. "I've been fortunate to work closely with so many scientists and researchers at Stanford whose groundbreaking research will undoubtedly lead to better treatments for cancers and allergies. In my opinion, they deserve all the recognition, and anything I can do to draw attention to the incredible work that they're doing — actually saving people's lives and making this world a better place — is an incredible honor."

Parker was ranked No. 5 on the Chronicle of Philanthropy's 2014 Philanthropy 50 list. He has won a number of awards for his public service activities, including the 2016 Roger Horchow Award for Outstanding Public Service from the Jefferson Awards Foundation. Parker was ranked No. 5 on the Chronicle of Philanthropy's 2014 Philanthropy 50 list. He has won a number of awards for his public service activities, including the 2016 Roger Horchow Award for Outstanding Public Service from the Jefferson Awards Foundation.

Funding research in cancer immunotherapy

Parker is a philanthropist and entrepreneur with a record of launching genre-defining companies and organizations. He is the founder and president of the Parker Institute for Cancer Immunotherapy to spur research on the relationship between the immune system and cancer. Stanford Medicine is one of the six participating institutions.

At 19, he co-founded the online file-sharing service Napster, and at 21 he co-founded Plaxo, an online address book. In 2004, he joined Mark Zuckerberg to develop the online social network Facebook, and he served as Facebook's founding president. In 2007, he co-founded Causes on Facebook, which registered 180 million people to donate money and take action around social issues.

"I'd like to thank Dean Minor and the entire team at Stanford Medicine for this extraordinary recognition," Parker said. "I've been fortunate to work closely with so many scientists and researchers at Stanford whose groundbreaking research will undoubtedly lead to better treatments for cancers and allergies. In my opinion, they deserve all the recognition, and anything I can do to draw attention to the incredible work that they're doing — actually saving people's lives and making this world a better place — is an incredible honor."

Parker was ranked No. 5 on the Chronicle of Philanthropy's 2014 Philanthropy 50 list. He has won a number of awards for his public service activities, including the 2016 Roger Horchow Award for Outstanding Public Service from the Jefferson Awards Foundation. Parker was ranked No. 5 on the Chronicle of Philanthropy's 2014 Philanthropy 50 list. He has won a number of awards for his public service activities, including the 2016 Roger Horchow Award for Outstanding Public Service from the Jefferson Awards Foundation.
An inflammation test that may predict cardiovascular disease

By Bruce Goldman

A blood test devised by School of Medicine scientists spits out a single number that strongly predicts the development of the world’s most prevalent medical disorder: cardiovascular disease.

While more research remains to be done, there’s good reason to suspecting this test could help to predict many other diseases of old age, said Mark Davis, PhD, professor of microbiology and immunology. A paper describing the test was published online Oct. 13 in Cell Systems. Davis is the senior author. Lead authorship is shared by former postdoctoral scholars Shai Shen-Orr, PhD, who is now an assistant professor at Technion-Israeli Institute of Technology in Haifa, and David Furman, PhD, now a consulting associate professor at Stanford.

Mounting evidence suggests that many diseases that become more common with advancing age do so because the immune system begins to malfunction, said Davis, a Howard Hughes Medical Institute investigator and the director of Stanford’s Institute for Immunology, Transplantation and Infection.

In addition to responding more sluggishly to dangers such as infectious pathogens or incipient tumors, the aging immune system tends to spend its downtime — periods when it has no imminent challenge to respond to — in a low-grade inflammatory state. Medical experts are increasingly convinced that this constantly thumping, systemic, inflammatory activity threatens diverse tissues throughout the body.

A better test?

Cholesterol testing, a diagnostic mainstay, flags cardiovascular risk only about half of the time, said Davis, who is also the Burt and Marion Avery Family Professor. "For too many men experiencing a heart attack or stroke, the first observed hint of cardiovascular risk is their death," he said.

Testing for levels of CRP, a circulating protein linked to cardiovascular disease, has been shown to further enhance the prediction of cardiovascular risk, even among patients with normal cholesterol levels. A CRP reading is relatively simple to get, requiring only a blood draw and relatively straightforward lab tests.

The new test developed by the Stanford researchers is more complicated but appears to have superior diagnostic value to either the cholesterol or CRP test. Rather than testing circulating inflammatory proteins, it tests for the response of immune cells themselves to inflammation — a signal that appears to be more stable and hence a more robust diagnostic. In the study, it was able to detect early cardiovascular irregularities in otherwise relatively straightforward lab tests.

The new test developed by the Stanford researchers is more complicated but appears to have superior diagnostic value to either the cholesterol or CRP test. Rather than testing circulating inflammatory proteins, it tests for the response of immune cells themselves to inflammation — a signal that appears to be more stable and hence a more robust diagnostic. In the study, it was able to detect early cardiovascular irregularities in otherwise asymptomatic individuals.

The researchers took advantage of data from the first three years of what was to become a nine-year longitudinal project carried out at Stanford under the direction of study co-author Cornelia Dekker, MD, a professor of pediatric infectious disease. In all, 90 adults, divided into two groups — people younger than 40 and people older than 60 — were assessed annually at high risk of infection with a battery of tests as to the state of their immune system, how it varied from year to year within and between individuals and how this related to clinical markers of inflammation.

Isolating immune cells

For the Cell Systems study, the researchers isolated several types of immune cells from individual blood samples and measured these cells’ responses to stimulation by circulating signaling proteins called cytokines. Many cytokines tend to shift the immune system into high gear.

The investigators recorded the extent to which several different types of immune cells mixed with cytokines in a lab dish increased the activation of intra- cellular substances called STAT proteins. In response to this stimulation, STAT proteins are known to undergo small chemical changes, causing them to head into a cell’s nucleus and turn on batteries of genes that stir the cell’s quiescent cell into a frenzy of immunological activity.

When immune cells from young people were stimulated with certain cytokines, the activation levels of STAT proteins skyrocketed. When the same thing was done to immune cells from old people, STAT-protein activity rose a lot less.

However, pre-stimulation levels of STAT-protein activation in immune cells from old people were substantially higher than in those from young people, suggesting that older people’s immune systems are constantly somewhat revved up when they should be at rest.

Still, older people’s pre-stimulation STAT-protein activation levels, and these proteins’ activation in response to cytokine stimulation, varied widely between individuals. Some showed few signs of it, while in others it was pronounced.

A blood test developed by Mark Davis and his colleagues may be able to predict the development of cardiovascular disease.

The investigators blended 15 separate cytokine-responsive measurements to generate a single number called a cytokine response score. This measure, which varied considerably among different older adults, was assailable from year to year in the same individual. A higher CRS is better, as it indicates a more-responsive immune system and lower background inflammation. For example, individuals taking fish oil had higher CRSs. (Fish oil is known to have anti-inflammatory properties.) No other drug tested showed this correlation.

Cross-referencing cytokine response scores

At the suggestion of study co-author François Hadji- dimitriou, MD, a clinical associate professor at Stanford’s cardiovas- cular medicine, the cytokine response score of each of 40 older subjects was then cross-referenced against cardio- vascular health assessments carried out up to two years later. These assessments included a comprehensive clinical history and tests of arteriosclerotic plaque, arterial stiffness and ventricular function.

Of the 40 subjects, 18 were in good cardiovascular health. Ten had already suffered cardiovascular events, and seven had sufficient arteriosclerosis to be considered subclinical. Five others had lesser signs of cardiovascular problems and were considered borderline.

The researchers found that cytokine response scores were inversely correlated with clinical signs of arteriosclerosis and with two measures associated with the heart’s ability to relax between beats. Importantly, the borderline subjects also had higher cytokine response scores. The scores’ predictive value exceeded that of CRP tests, the current standard for measuring inflammation-based cardiovascular risk.

For now, the test to obtain a cytokine response score is not available in clinics; it’s too complex and expen- sive. Davis said he and his colleagues want to try to simply and drive down the cost.

“The CRS may be a useful proxy for healthy aging,” said Davis. "And its predictive accuracy in cardiovascu- lar disease further substantiates the inflammatory underpinnings of that prevalent, age-related condition.”

The team’s work is an example of Stanford Medi- cine’s focus on precision health, the goal of which is to anticipate and prevent disease in the healthy and pre- cisely diagnose and treat disease in the ill.

Other Stanford co-authors of the study are former research assistant Brian Kidd, PhD, now at the Icahn School of Medicine at Mount Sinai in New York City; research and development engineer Patricia Lovelace; research assistant Yin-Wen Huang; Yael Rozenberg Has- son, PhD, immunosyssay and technical director at the Institute for Immunity, Transplantation and Infection; Sally Mackey, associate director of the Stanford-LPCH Vaccine Program; Armanan Gisard, MD, research fel- low at the Stanford Cardiovascular Institute; associate professor of microbiology and immunology Holden Maecker, PhD, associate professor of the Stanford Institute for Aging Research; Chih Huang, PhD, professor of immunology Yue-Hsien Chien, PhD; professor of radiology Joseph Wu, MD, PhD; and former associate professor of medicine Arul Burte, MD, PhD, now at the Univer- sity of California-San Francisco.

The study was funded by the National Institute of Allergy and Infectious Diseases, the Ellison Medical Foundation, the Howard Hughes Medical Institute, the Israeli Science Foundation, the Stanford Cardiovascular Institute and the Stanford Center on Longevity.

Stanford’s Department of Microbiology and Immuni- nology also supported the work.

Two researchers receive funding from BRAIN Initiative

Two School of Medicine research- ers are among the recipients of the third round of grants from the National Insti- tutes of Health’s BRAIN Initiative, which has awarded more than $70 million, are being given this year to over 170 investigators work- ing at 60 institutions. These awards ex- pand NIH’s efforts to develop new tools and technologies to understand neural circuit function and capture a dynamic view of the brain in action. The initiative was launched in 2014.

The two Stanford recipients are Vinod Menon, PhD, professor of psychia- try and behavioral sciences, and Kim Butts Pauly, PhD, professor of neurology. Menon received $387,000 from the NIH’s National Insti- tute of Biomedical Imaging and Bioengineering for a project titled “Novel Bayesian linear dynamical systems-based methods for dis- covering human brain circuit dy- namics in health and disease.” He and his colleagues plan to develop novel algo- rithms for identifying dynamic functional networks in the brain and characterizing network interactions between brain re- gions involved in cognitive tasks.

Butts Pauly received $939,000 from the NIH’s National Institute of Neurological Disorders and Stroke for a project titled “MR-guided focused ultrasound neuromodulation of deep brain structures.” Through this work, she hopes to develop noninvasive technology that combines focused ultra- sound neuromodulation for therapeutic purposes with magnetic resonance im- aging to accurately predict ultrasound intensities and temperatures at the target site and throughout the brain.

http://bloodcenter.stanford.edu

PleASe givE BDooTH lineage needed O-, B- and AB-

To request an appointment, call 723-7631 or you can make an appointment online.

33333 Health Ave., Palo Alto
415 Burgundy Drive, Menlo Park
515 South Dr., Mountain View

To request an appointment, call 723-7631 or you can make an appointment online.

33333 Health Ave., Palo Alto
415 Burgundy Drive, Menlo Park
515 South Dr., Mountain View
http://bloodcenter.stanford.edu

To request an appointment, call 723-7631 or you can make an appointment online.

33333 Health Ave., Palo Alto
415 Burgundy Drive, Menlo Park
515 South Dr., Mountain View
http://bloodcenter.stanford.edu

To request an appointment, call 723-7631 or you can make an appointment online.

33333 Health Ave., Palo Alto
415 Burgundy Drive, Menlo Park
515 South Dr., Mountain View
http://bloodcenter.stanford.edu

To request an appointment, call 723-7631 or you can make an appointment online.

33333 Health Ave., Palo Alto
415 Burgundy Drive, Menlo Park
515 South Dr., Mountain View
http://bloodcenter.stanford.edu
A dietary approach to depleting blood stem cells may make it possible to conduct bone marrow transplants without the use of chemotherapy or radiation therapy, according to researchers at the School of Medicine.

The discovery, made in collaboration with researchers at the University of Tokyo, may also become a new treatment for certain cancers without chemo or radiation, which can cause severe side effects.

The researchers showed that a diet deficient in the essential amino acid valine could effectively deplete the population of blood stem cells in mice and allow them to be successfully transplanted with blood stem cells from other mice. The researchers also showed that human blood stem cells in the laboratory were affected by a lack of access to valine, suggesting that the same therapeutic approach may work in humans.

A paper describing the findings was published online Oct. 20 in Science. The lead author is Yuki Yamauchi, a former graduate student at the University of Tokyo. The senior authors are Hiromitsu Nakauchi, MD, PhD, a professor of genetics at Stanford, and Satoshi Yamazaki, PhD, an associate professor at the Center for Stem Cell Biology and Regenerative Medicine at the University of Tokyo.

Effects of valine-deficient diet

“Bone marrow transplantation is a toxic therapy,” said Nakauchi, who is also a member of Stanford’s Institute for Stem Cell Biology and Regenerative Medicine.

“We have to do it to treat diseases that would otherwise be fatal, but the quality of life afterward is often not good.”

He added, “Relative to chemotherapy or radiation, the toxicity of a diet deficient in valine seems to be much more. Mice that have been irradiated look terrible. They can’t have babies and live for less than a year. But mice given a diet deficient in valine can have babies and will live a normal life span after transplantation.”

The effect of a valine-deficient diet is fairly specific to blood stem cells, but there seem to be other sorts of stem cells that may be affected, Nakauchi said, including hair stem cells and some T cells. Other types of stem cells may also be affected, but the effects are not nearly as widespread or extreme as those caused by chemotherapy or radiation therapy, he said.

Nakauchi, who is also an investigator at Stanford’s Ludwig Center for Cancer Stem Cell Research, and the National Institute of Health’s Intramural Research Program, said, “All of our valine has to come from our diet; otherwise we would otherwise starve to death.”

“The lightbulb moment,” Nakauchi said, came after he read the work of Christian Kornberg’s 1946 research that certain types of anemia in rats could be cured by giving them mixtures of purified amino acids.

The discovery, made in collaboration with researchers at the University of Tokyo and the University of Pennsylvania, may also become a new treatment for certain cancers without chemotherapy or radiation therapy, according to researchers at the School of Medicine and the University of Tokyo.

The senior authors are Hiromitsu Nakauchi, MD, PhD, a professor of genetics at Stanford, and Satoshi Yamazaki, PhD, an associate professor at the Center for Stem Cell Biology and Regenerative Medicine at the University of Tokyo.

A paper describing the findings was published online Oct. 20 in Science. The lead author is Yuki Yamauchi, a former graduate student at the University of Tokyo. The senior authors are Hiromitsu Nakauchi, MD, PhD, a professor of genetics at Stanford, and Satoshi Yamazaki, PhD, an associate professor at the Center for Stem Cell Biology and Regenerative Medicine at the University of Tokyo.

Common prostate cancer treatment linked to later dementia

By Christopher Vaughn

A 1946 paper by the late Arthur Kornberg led Hiro Nakauchi and his colleagues to discover that removing valine, an essential amino acid, from the diet of mice depleted their blood stem cells.
Growing up in a hospital: My 25 years with Packard Children’s

By Misty Blue Foster

For most people, the trajectory is clear: When you are a kid and you’re sick, you go to the pediatrician. If you have a chronic medical condition, as in my case, you establish a team of pediatric specialists who can provide for your health issues on a consistent basis throughout your childhood. As you get older, you work with these specialists to transition your care to a new team of doctors who are better suited for treating adults.

For me, however, this hasn’t been the path. I am 30 years old, and I am still an active patient at Lucile Packard Children’s Hospital Stanford. My conditions are so complex that they require the care of specialists who have been with me since early childhood. Beyond my medical care, these specialists have been committed to me in a bigger way: They have become my family, which is something I truly did not know until I found myself in the hospital.

Finding my voice

I was born prematurely to a heroin-addicted mother. I was diagnosed with spina bifida and cloacal exstrophy, a rare birth defect of the abdominal wall in which the organs are outside of the body. These conditions come with a host of related medical complexities, which led to frequent, unplanned hospitalizations throughout my childhood.

My mom spent much of my early years in and out of prison, where she passed away when I was just 5 years old due to health issues from her years of drug abuse. After her death, I was permanently placed in foster care, and this was the beginning of a long, painful chapter of my life. I spent 14 difficult years in the system. During this time, I was deprived of the medical care that I needed at home, and I was exposed to gangs, homelessness, drugs, alcohol, and neglect, including extremely unsanitary living conditions.

As a result, I developed frequent infections that often required hospitalization. Over the years, I have had more surgeries than I can count to maintain function in my bowels, bladder, spine, pelvis and hips. For my frequent inpatient stays, my foster mom would check me in to the hospital and then leave. I’d hear other families talking and laughing and soothing their children in the neighboring rooms as I sat alone, with only the sounds of the beeping and whirring of the machines for company. This experience taught me to advocate for myself and to ask questions that could be part of the decisions for my own care.

Growing up at Packard Children’s

My nurses and doctors were impressed by my precocity and concerned about my lack of parental support, so they went above and beyond and gave me what felt like a family. They were some of the first adults in the world who respected my voice and made me feel safe, welcome and deserving of a good chance in life.

One nursing assistant in particular, Petie Core, now retired, would visit with me for hours after her shifts ended. She would bring me my favorite snacks and take me on walks around the hospital. Today, Petie remains a huge part of my life. She and her late husband gave me away at my wedding in 2006, and I even call her “Mom.”

I also have Packard “grandparents.” I met Grandpa Dave Olsen when, as a volunteer, he came to read stories to me, something he dedicated himself to after losing his own grandson to cancer. I explained to him that I was alone, and he assured me, “I’ll be your grandpa.” He kept true to his promise, and in the years that followed we stayed close, sharing holidays and life milestones.

Pursuing my dreams

As I got older, I expected to phase out of the children’s hospital. When I was in my 20s and married, I started to see adult specialists. But I always came back to Dr. William Kennedy (a professor of urology) and his team at Packard Children’s. They knew my story and my medical history, and they were able to treat my congenital complexities, which adult specialists have struggled to navigate. Also, I’ve always felt this was a place where my voice was respected, no matter how big my dreams became as I thought about my future outside the hospital walls.

Thanks to the care and encouragement I received at Packard Children’s, I was inspired to pursue my dream of becoming a nurse. When administrators reviewed my nursing school application and doubted whether I was physically capable of such a demanding job, my doctors convinced them otherwise. “She can walk, talk, think and do everything like the rest of the applicants can. She just may have to go to the bathroom more often than some others,” Kennedy told the schools.

It paid off. Today I am a licensed vocational nurse at the Veterans Affairs Palo Alto Health Care System where I work in the medical specialty clinic, caring for patients in the cardiology, urology and neurology units. I also work in Blind Rehabilitation Services with veterans who have lost their vision due to disease or blindness, and I am pursuing my master’s degree in public health at San Jose State University.

I’ve paved the way for myself, and I hope that through my work as a nurse I will be able to pay forward the extraordinary care I’ve experienced throughout my life. I’ve always said, “You can’t always control what you are given in life, but you can control what you do with it.” I’m striving for that every day.

Misty Blue Foster is a licensed vocational nurse at the Veterans Affairs Palo Alto Health Care System.

Foster at age 6 during a stay at Packard Children’s.

Foster with William Kennedy, a Stanford urologist who cared for her.

Foster with Petie Cole, a retired nursing assistant at Packard Children’s, after Foster’s Skyline College graduation ceremony.

The new retrospective study of patient records took only a few weeks, said Shah. “We are working to make such studies as simple as a Google search,” he said. “We were down to weeks in this one, geared out efforts, which are funded by the Dean’s Office, have gotten us to close to two to three days.”

In contrast, a prospective, randomized clinical trial to establish whether ADT can be more effective than placebo in treating dementia would require many millions of dollars, said Kenneth Mahaffey, MD, a Stanford professor of medicine who was not involved in the study.

Studies of existing patient health records are far cheaper and faster than “gold standard” randomized, clinical prospective studies. And patient health record studies offer powerful ways to identify hypotheses about efficacy and safety that are worth further testing in clinical trials, said Mahaffey, who is vice chair of clinical research in Stanford’s Department of Medicine.

But the lack of randomization in health record studies means the results can be misleading, cautioned another of the study’s joint authors, G. William McPhee, MD.

In his research was supported by the National Library of Medicine and the National Institute of General Medical Sciences. Stanford’s Department of Medicine also supported the work.

Shah has three pending patents on effective ways to mine electronic health records data.
They’re told, ‘Here’s a little Valium. I think you’re anxi-
ous.’ They get belittled, not taken seriously, and they get really depressed.”

Unroofing

Unroofing the myocardial bridge entails cutting through the heart muscle to uncover the tunneled ar-
tery, thus relieving compression on the artery caused by the brid-
ging. The surgery is known to be effective, Boyd said. However, concerns that healthy heart mus-
cle could be damaged during the operation have slowed its adoption. “In this study, we use new imaging techniques to map the bridge muscle very precisely, and we perform the unroofing with conservative surgi-
cal techniques to safeguard the healthy heart muscle,” he said.

In the past, the surgery was done only as a treatment of last resort, Schnittger said. “You took a patient very, very occasionally to surgery when everybody had tossed their hands up,” she said. “Stanford probably did no more than one surgery a decade in the past.”

But with Schnittger and her team, including study co-author Tremmel, MD, assistant professor of cardiovascular medicine, and Ian Rogers, MD, clinical assistant professor of cardiovascular medicine and of pediatric cardiology, helping to guide the surgeries, the number performed at Stanford Medicine has increased substantially. More than 80 have been performed at SHC and Lucile Packard Children’s Hospital Stan-
ford in the past five years.

For the new study, the research-
ers examined 50 adult patients who between 2011-15 underwent the unroofing procedure because of severe symptoms that medication had failed to manage. The first 35 were performed at Stanford while the other 15 were performed off-pump on a beating heart.

Studying the condition in the lab

We studied the patients’ hearts comprehensively in the lab, proving there was ischemia when we simulated a stress test by infusing drugs that increased the heart rate,” Schnittger said. “Increased heart rate, anxiety, sleep deprivation — anything that drives up the heart rate would also cause ischemia.”

Prior to surgery, study participants filled out the Se-
attle angiography questionnaire, a three-page survey describ-
ing their symptoms and ranking their quality of life. Then six months after the surgery, they filled out the survey again.

This is a comprehensive survey often used in cardiac research to ask how much pain the patient has, how fre-
quently they have it, how much it limits their life.

Results showed that the average rank-
ing of quality of life prior to surgery by the patients was 25 percent. After surgery, that figure jumped to 78 percent.

“Before surgery was complete, you couldn’t get them to do much,” Schnittger said. “They have suffered for so long — finally they’ve found doctors who understand them.”

“One patient, a mother of five, was so sym-
mptomatic before surgery she had ar-
ranged her whole life around her symp-
toms. She didn’t play with her children outside; she couldn’t even pick them up at the playground. She was basically housebound. She couldn’t do laundry or go grocery shopping. After surgery, she could do all those things — laundry, play outside with her children, go for a walk. It’s a life-changer.”

“Our team wants to spread the word, to educate the medical community that this is a real thing,” she added, noting that a myocardial bridge clinic has been estab-
lished at Stanford. “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 diag-
ose and treat disease in the ill.”

Other Stanford co-authors are postdoctoral scholar Vedant Pargankar, MD, resident David Scoville, MD, Takumi Ikuma, MD, PhD, Shigemitsu Tanaka, MD, PhD, and Ryoitomo Yamada, MD, PhD, all members of the Stanford University Cardiovascular Core Analysis Laboratory; Michael Fischbein, MD, PhD, associate profes-
sor of cardiothoracic surgery; and R. Scott Mitchell, MD, professor emeritus of cardiothoracic surgery.

Stanford’s departments of Medicine and of Cardio-
 thoracic Surgery supported the work.

By Jennie Dusheck

Frank Graham Sommer, MD, a professor emeritus of radiology at the School of Medicine and an accom-
plished pianist, died Oct. 2 of amylo-
oid-sclerotic cardiac arrest at his home in the Stanford campus. He was 70.

An expert in ultrasound imaging and other radiological imaging tech-
niques, Sommer received the 1966

Academy of Radiology Research’s Dis-
tinguished Investigator Award. His ge-
nerous personality helped create a warm and collegial professional environment in the medical school’s Department of Radiology, said colleague Michael Federle, MD, a professor of radiology. “He always lived life to the fullest,” said Federle. Sommer was born in Victoria, Brit-
ish Columbia, in 1946. He earned a bachelor’s degree in physics from the University of Victoria and a medi-
cal degree from McGill University in Mon-
tréal. He joined the faculty at Stanford in 1979.

A ‘Renaissance radiologist’

Sommer had wide-ranging interests in his field, humorously characterizing himself as a “Renaissance radiologist.” He studied and promoted improved imaging techniques and is known for his work on ultrasound and imaging blood flow in the kidneys.

“He was a driven man,” said his wife, Denise Leclair. “He had such a hungry mind; it drove him.”

But he didn’t conform to the stere-
type of the scientific, num-

nptiapient scientist, she said. Sommer was adventurous, thoughtful, kind, gener-
uminous and charming, she said. He was also very logical and a careful plan-
er, she said. “But then he would say something, and it would just stop the conversation and make you laugh.”

When not at work, he would often play the piano for audiences at Filipi, an eatery in Woodside that’s open to the public, and at restaurants and se-

tor centers — favoring classical, pop-
ular and ragtime music.

Sommer recently pledged $1 mil-
lion to McGill University to fund a Ca-

nadian-wide competition for com-
posers. The competition, intended to

support composers under age 35 and to promote the creation of new musi-
cal collaborations in 2017.

Besides his work and his music, Sommer enjoyed biking, skiing and windsurfing, as well as playing tennis, golf, racquetball and squash.

Federle called him a “tremendous athlete.” In a typical experience play-
ging golf with Sommer, said Federle, Sommer would show up to tee off, having already taken a 20- or 30-mile mountain bike ride. “Then he’d walk 18 holes of golf.”

Leclair said Sommer planned ev-


imgly he did care fully, carrying his research habits into his daily life. In 1995, when Sommer and Leclair had hardly met, she recalled: “We were making a recipe of salmon in filo dough.” It was his habit to make a recipe many times, slightly altering the recipe each

time until he thought it was perfect, she said. But Leclair impulsively de-
cided to throw some blackberries in-
side the filo dough with the salmon.

“He was astounded!” Leclair laughed. And he never forgot that she had done that, saying, “I could tell by his face how much he enjoyed it.”

In addition to Leclair, Sommer is survived by a sister, Anne Oxford, of West Vancouver, British Columbia. A celebration of his life will be held at 1 p.m. Oct. 28 at Alta Mesa Funeral Home, 695 Ararat Road, Palo Alto.
Antidepressants continued from page 1

MRT scans and questionnaire

"Currently, finding the right antidepressant treatment is a trial-and-error process because we don't have precise tests," Williams said. "For some people this process can take years. As a result, depression is now the leading cause of disability worldwide." For the trial, the researchers conducted brain scans on 80 participants with depression. Participants lay in a functional MRI machine while viewing images of happy faces and fearful faces on a screen in front of them. Each face triggered brain circuits involving the amygdala, an almond-shaped structure linked to the experiencing of emotions.

The scans were conducted both before and after an eight-week treatment period with three commonly used antidepressants: sertraline (Zoloft), escitalopram (Lexapro) and venlafaxine (Effexor). Participants also completed a 19-item questionnaire on early life stress, which assessed exposure to abuse, neglect, family conflict, illness or death (or both), and natural disasters prior to the age of 18.

The researchers analyzed the pretreatment imaging and the questionnaire to determine how the individual patients would respond immediately after the eighth week. "Our predictions were correct," Goldstein-Piekarski said.

A statistical analysis called predictive modeling, study results showed that participants exposed to a high level of abuse trauma were most likely to recover with antidepressants if the amygdala was reactive to the happy faces. Those with high levels of childhood trauma whose amygdala showed low reactivity to the happy faces were less likely to recover with antidepressants.

"We were able to show how we can use an understanding of the whole person — their experiences and their brain function and the interaction between the two — to help tailor treatment choices," Williams said. "We can now predict who is likely to recover on antidepressants in a way that takes into account their life history."

Effects of childhood trauma

Childhood trauma can change both the structure and function of the amygdala in ways that can affect the rest of a person's life, the researchers said. "For those whose amygdala is affected by early life stressors, there are different ways of responding to treatments and perceiving the world," Goldstein-Piekarski said.

For example, a child experiencing abuse by a caregiver learns to be hypervigilant and very aware of both the present and past emotions. As a result, the amygdala becomes hypersensitive to these emotions. And that's useful at that time.

"Unfortunately, sometimes the amygdala maintains this hypersensitivity & reactivity in later life, but it changes slightly," Andrea said. "As an adult, they lose out on that ability to respond to the more positive emotions."

By using functional MRI to examine the emotional circuitry of the brain — the neural circuit that responds to emotions and trauma — the researchers quantify how early childhood trauma affected the brain. Those participants whose emotional brain retained the capacity to respond well to positive emotions — the happy faces in the fMRI test — had good chance of recovering with antidepressants, the researchers said. "For those patients who have lost this capacity, putting them down an antidepressant path is likely to cause more heartache," Williams said. "That's when you would consider other types of treatment. First, treat the effects of the childhood trauma through methods such as trauma-informed psychotherapy, and then consider antidepressants."

Recommendation: Order brain scan

The researchers say results from this study could be useful for physicians who usually provide the first line of treatment for patients with depression. They envision the integrative clinical approach in which physicians ask about childhood trauma and order a five-minute brain scan to help determine the best line of treatment.

"If we are thinking about trying to get this right the first time, it's useful to consider the option of ordering a scan," Williams said. "It's already done for so many other things — a broken leg, a heart problem, a potential tumor."

The study also provides a table that the researchers say could ultimately be used by practicing physicians to determine the threshold at which antidepressant treatment is recommended depending on the varying levels of childhood trauma and brain-scan results from patients.

"We interacted with a lot of primary care providers during this study — about 200 of them," Williams said. "The practitioners themselves like the idea of a scan. They want to know who is likely to benefit from antidepressants, and when they should refer for specialist psychiatric services including psychotherapy. Currently, there is nothing to help them make that decision."

Today, if the first line of treatment doesn't work, patients spend an average of two to three years going through trial-and-error personal before getting treatment that helps, Williams said. She added that by that time, the disability burden has increased tremendously, with lost productivity of up to $14,000 a year per employee, not to mention the patient's suffering continues while the disease progresses.

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 of the study are postdoctoral scholar Erin Green, PhD; Trisha Suppes, MD, PhD, professor of psychiatry and behavioral sciences; Alan Schatzberg, MD, professor of psychiatry and behavioral sciences; and Trevor Hastie, PhD, professor of statistics.

The study was funded by Brain Resource Pty. Ltd. and by grants from the National Institute of Mental Health. Williams has received consulting fees from Brain Resource Pty. Ltd. and Stanford's Department of Psychiatry and Behavioral Sciences also supported the work.

Hadron continued from page 1

Unlike photons or electrons, which release energy along the entire path of their path, the charged particles deliver most of their damaging energy in one burst inside the tumor. They are more effective at damaging DNA in- sided cancer cells, and some studies have suggested they can effectively incite an immune response against the tumor. Charged particle beams can also be shaped to treat tumors of various sizes and shapes.

There are about 10 carbon-based hadron therapy centers in the world, but none in the United States. "The center is expected to be located on the grounds of the VA-Palo Alto," said Dexter McCormick, professor of radiation oncology at the School of Medicine and the Katharine Dexter McCormick Professor. "I believe particle beam therapy will transform the care of cancer in this country. We will have the potential to eradicate radio-resistant tumors. In addition, we hope to also use this approach to boost the survival and decrease the toxicity experienced by patients with large-volume metastatic disease. Our goal is to improve the survival of patients who are cur- rently considered incurable."

In addition to treating veterans, physicians at the center would also treat nonveterans and children with cancer.

"Lucile Packard Children's Hospital and Stanford Medicine have long been at the vanguard of pediat- ric care and scientific discovery to improve the lives of children," said Christopher Dawes, president and CEO of Lucile Packard Children's Hospital Stanford and Stanford Children's Health. "Planning for the hadron center, which provides proton and heavier charged par- ticle therapy, is no exception. It will change the way we fight cancer and reduce late toxicity in pediatric and young adult patients."

The center also will be used to conduct research and clinical trials to validate the potential of hadron therapy in cancer patients and to miniaturize the technology (in collaboration with the SLAC National Accelerator Laboratory) to make it more affordable and accessible for cancer patients around the world.

"We at Stanford Medicine have been working on this for several years and are thrilled that we will have the opportunity to work with the Palo Alto VA to bring the nation's first hadron therapy system to Stanford," said Shridhar Sethuraman, vice president for cancer services at Stanford Health Care. "We believe that Stanford Medicine has the innovative spirit and the expertise to refine, test and validate this technology for the benefit of our patients."
Mark Cullen tapped to be senior associate dean for research

By Ruthann Richter

Mark Cullen, MD, director of the Stanford Center for Population Health Sciences, has stepped into a new role as senior associate dean for research at the School of Medicine.

Cullen will share the responsibilities of the job with Harry Greenberg, MD, the current senior associate dean for research, until June 2017. Greenberg will stay on after that time in a newly created position of associate dean for research.

“Dr. Cullen came to Stanford in 2009 to serve as chief of medical disciplines and quickly earned a reputation as a compassionate clinician, respected mentor and collaborative colleague,” Lloyd Minor, MD, dean of the School of Medicine, said in announcing the appointment Oct. 5.

A distinguished scientist and public health expert, Cullen said one of his goals is to build the stature of Stanford’s program in quantitative sciences, or what he calls the dry-lab sciences.

Promoting dry-lab sciences

“One of my major ambitions in the new job is to advance the science culture,” said Cullen, who is also a professor of medicine. “I want people to accept the potential of dry-lab research to be an equal partner with what is historically been fantastic at Stanford, which is lab-based science.”

Cullen said he wants to foster an environment in which social scientists and biostatisticians work collaboratively with basic science researchers. He is also committed to improving the research infrastructure of Spectrum Children’s Hospital, where he has been on the faculty for the past 15 years.

“My mission is to improve the culture of research at Stanford,” Cullen said. “I want people to accept the potential of research methods other than traditional lab-based research.”

Cullen starts his new role immediately and will be a full-time faculty member in the Department of Pediatrics and an associate professor of medicine, effective Sept. 1.

His research uses single-molecule microscopy to understand how noncoding sequences in the genome interact functionally. His research methods have been supported by many grants including the National Institutes of Health, the March of Dimes and the American Heart Association.

A native of Chicago, Cullen completed his medical degree at the University of Chicago and completed his residency in pediatrics at the University of Pennsylvania.

His laboratory and clinical research focus on understanding the biology of Alzheimer’s disease in premature and newborn babies.

“Throughout his tenure, Dr. Greenberg has been a champion for increased collaboration across the research spectrum and across disciplines around the university,” Minor said. “He played a key role in helping to expand PI waiver privileges to clinician-educators and postdoctoral fellows, and I have deeply appreciated his wise counsel and many contributions to Stanford Medicine and the university.”

In announcing the appointment, Minor also praised Greenberg, a professor of medicine and specialist in Post-Traumatic Stress Disorder.

Greenberg, a professor of medicine and specialist in Post-Traumatic Stress Disorder at Stanford, will serve as the sole lead investigator following the grant’s renewal.

Sylvester named an associate dean for maternal and child health

By Erin Digita

Karl Sylvester, MD, has been appointed associate dean for maternal and child health to teach at the School of Medicine.

An associate professor of surgery and of pediatrics, Sylvester takes over the position from Mary Leonard, MD, who is now chair of the Department of Pediatrics at Lucile Packard Children’s Hospital.

He joins three other associate deans for maternal and child health who represent faculty affairs, global affairs and obstetrics.

“We are delighted to welcome Karl to his new role,” said Lloyd Minor, MD, dean of the School of Medicine. “He is an accomplished clinician, mentor and researcher who will bring his expertise in all of these arenas to the job of advancing scientific investigation in child and maternal health.”

Working in concert with co-associate deans for research Mark Cullen, MD, and Harry Greenberg, MD, Sylvester will focus on aligning the pediatrics and maternal research portfolios of the School of Medicine. He will also serve as a co-leader of Spectrum Child Health along with Leonard and David Stevenson, MD, senior associate dean for maternal and child health.

His laboratory and clinical research focus on understanding the biology of disease in premature and newborn babies. Sylvester has established a network of academic children’s hospitals and investigators to discover and test specific molecular diagnostistics of newborn diseases, such as necrotizing enterocolitis and sepsis. He is widely published on the clinical care of necrotizing enterocutitis and on his group’s findings on biomarkers of disease.

Sylvester earned a medical degree from Jefferson Medical College in Philadelphia and completed his clinical training at the University of Pennsylvania, Yale-New Haven Children’s Hospital and the Children’s Hospital of Philadelphia.

His laboratory and clinical research focus on understanding the biology of disease in premature and newborn babies. Sylvester has established a network of academic children’s hospitals and investigators to discover and test specific molecular diagnostistics of newborn diseases, such as necrotizing enterocolitis and sepsis. He is widely published on the clinical care of necrotizing enterocutitis and on his group’s findings on biomarkers of disease.