INSIDE STANFORD MEDICINE

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Over her years as a patient, Misty Blue Foster has found kindness and encouragement at the children's hospital.

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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 flashback," 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 significant relief for patients with myocardial bridges who have 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 See UNROOFING, page 6

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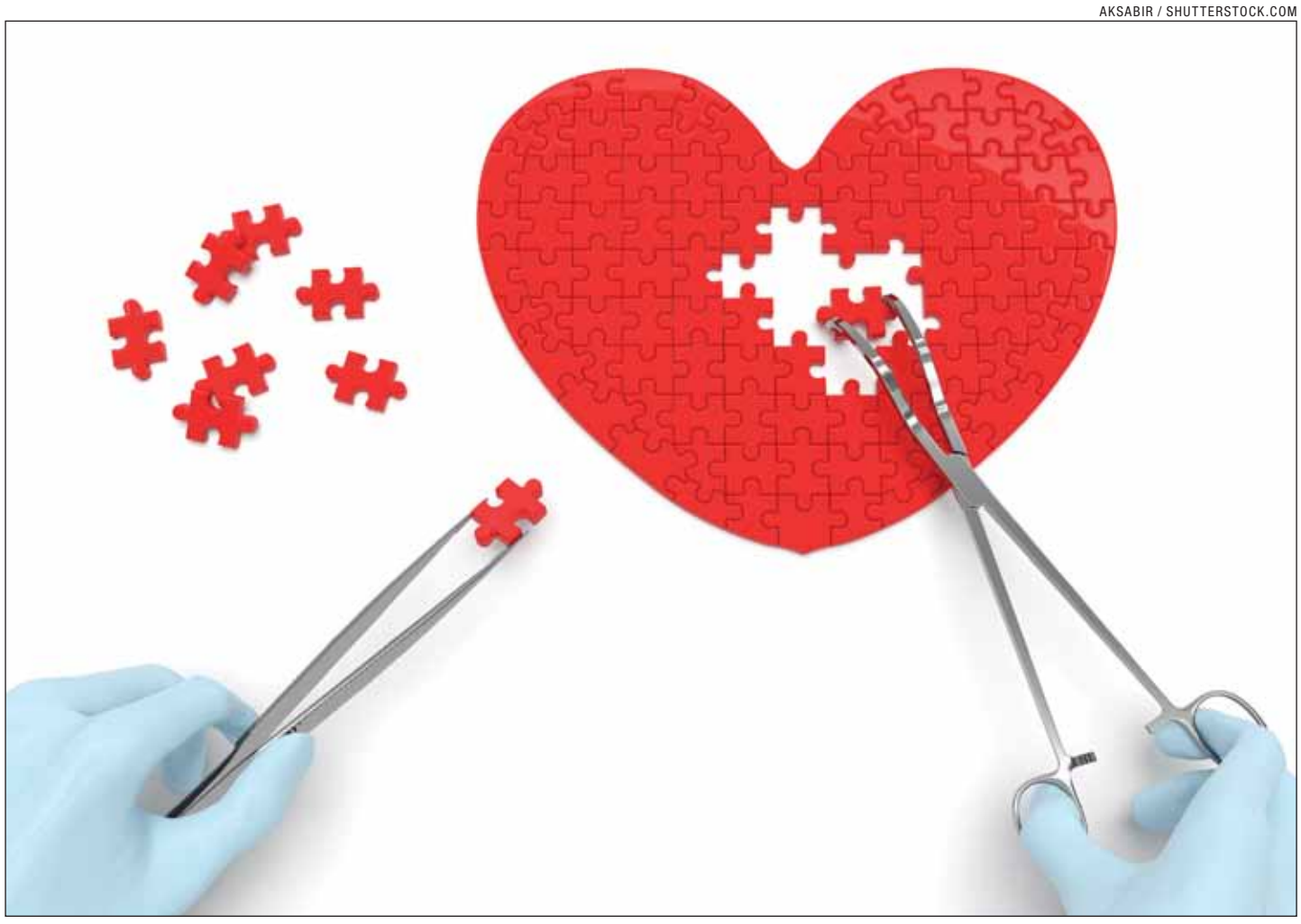

Stanford Medicine, VA will collaborate to build nation's first hadron therapy center

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.

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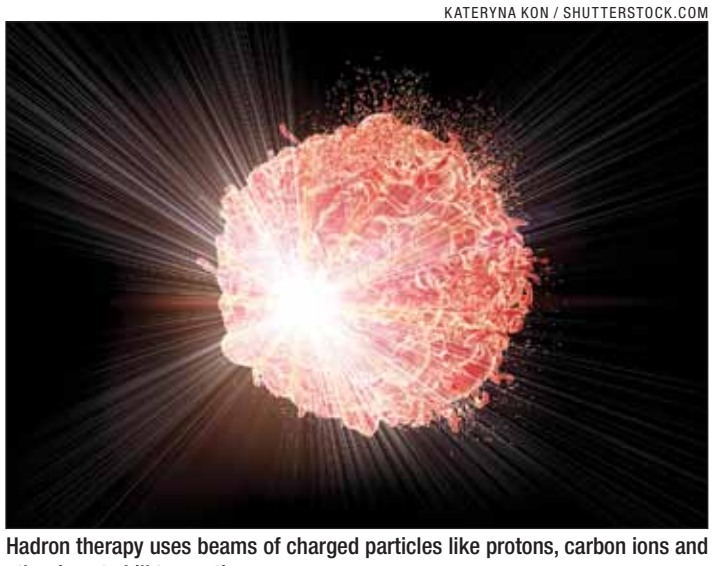

Hadron therapy uses beams of charged particles like protons, carbon ions and other ions to kill tumor tissue.

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. See HADRON, page 7

Researchers predict with high accuracy if antidepressants will help

By Tracie White

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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. 10 in the *Proceedings of the National Academies of Science.* Williams is the senior author. Postdoctoral scholar Andrea Goldstein-Piekarski, PhD, is the lead author. See ANTIDEPRESSANTS, page 7

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 medal honors 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, skills and resources to helping solve some of our era's hardest health problems," said Lloyd Minor, MD, dean of the School of Medicine. "They are also pioneers advancing our biomedical revolution in precision health, making predictive, preventive and proactive care possible around the world."

Focus on pediatric infectious disease

Arvin has dedicated her career to focusing on infectious diseases in children, particularly the varicella zoster virus, which causes chickenpox and shingles. Her clinical studies, funded by the National Institutes of Health, helped contribute to the development of the chickenpox vaccine and the shingles vaccine. She served as the chief of pediatric infectious diseases at Lucile Packard Children's Hospital Stanford before being named a vice provost in 2006. In that capacity, she oversees Stanford's interdisciplinary research institutes, university research policies and the Office of Technology Licensing.

"As I think about my career and where I am now, I realize we have a new understanding and new tools to probe the questions of human health and, in my case, the questions of how viruses take over the human host and how it is that we have learned to live with them through our immune responses and other mechanisms. These present an endlessly fascinating set of questions," Arvin said. "There's always the opportunity to do the next experiment and to find out that you were right or wrong in your hypothesis."

Arvin has won many awards, but she said she was literally speechless when she received the call from Minor notifying her that she would be recognized with the school's highest honor.

"Receiving this Dean's Medal is such an unexpected and rewarding honor," said Arvin, who began her Stanford career as a postdoctoral scholar in infectious diseases. "I'm so grateful for this and for all of the opportunities I've had over these many years at Stanford."

Ann Arvin

John Levin

Sean Parker

From education to law

Levin was first drawn to Stanford by a program in the School of Education that allowed him to complete a master's degree in education while teaching at a local high school. He was then accepted to Stanford Law School, where he received his law degree in 1973. He said he views both teaching and law as a service — a way to impact society and help others, as well as to create opportunities and solve problems. He began a law partnership in San Francisco, Folger Levin LLP, with Stanford graduate Peter Folger 38 years ago. The firm focuses on transactions, dispute resolution and strategic advice for businesses, individuals and nonprofit organizations.

Levin has been involved in a wide array of community activities and served on many boards, including a 10-year term as a Stanford University trustee. In addition to chairing the Stanford Health Care board, he is a member of the board of directors of Lucile Packard Children's Hospital Stanford and served as convening co-chair of the recently concluded Campaign for Stanford Medicine.

"The various ways in which I'm involved at Stanford are great sources of satisfaction to me," he said. "I tremendously appreciate and enjoy my many colleagues around the campus. I have the privilege of meeting and working with the most interesting people, who are focused on what I consider to be important problems in thoughtful and serious ways. For me to be in a position to be in those conversations and to have some small impact in the direction of initiatives and decisions and programs is just a great joy and privilege. It's something I don't feel I should be honored for. I feel quite the opposite. I feel quite sincerely that it's of enormous benefit to my life."

"The award is a happy bonus," he added, "but I am really grateful to be engaged in all the remarkable things that Stanford Medicine is doing and all the aspirational notions that Stanford Medicine is moving toward."

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 Foundation, which focuses on three areas: life sciences, global public health and civic engagement. Earlier this year, the foundation announced a $250 million grant to launch 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 immunological 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. **ISM**

Five faculty members elected to National Academy of Medicine

Four professors at the School of Medicine and one at the School of Humanities and Sciences have been elected members of the National Academy of Medicine.

Christopher Garcia, PhD; Mark Krasnow, MD, PhD; Mark Musen, MD, PhD; Thomas Rando, MD, PhD; and Laura Carstensen, PhD, now number among the academy's 1,947 members and 146 international members.

Garcia is a professor of molecular and cellular biology and of structural biology, a Howard Hughes Medical Institute investigator and a member of the National Academy of Sciences. His research focuses on understanding and manipulating interactions between receptors and ligands, particularly in the fields of immunology, stem cell biology and neurobiology.

Krasnow is a professor of biochemistry, executive director of the Wall Center for Pulmonary Vascular Disease and an HHMI investigator. His research examines the development of lung tissue and the role of stem cells, the genetic origin of lung cancer and other lung diseases, and the neural circuits that control breathing and speech.

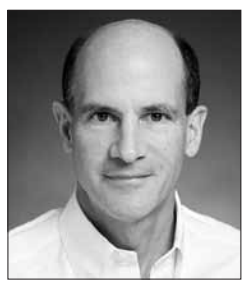
Musen is a professor of medicine and of biomedical data science and director of the Stanford Center for Biomedical Informatics Research. He is principal investigator for the Stanford Center for Expanded Data Annotation and Retrieval, which aims to make online biomedical data sets more accessible and reusable. His research focuses on intelligent systems, ontology engineering and biomedical decision support. He is a creator of Protégé, an open-source framework for building intelligent systems.

Laura Carstensen

Christopher Garcia

Mark Krasnow

Mark Musen



Thomas Rando

Rando is a professor of neurology and neurological sciences, director of the Glenn Center for the Biology of Aging and deputy director of the Stanford Center on Longevity. At the Veterans Affairs Palo Alto Health Care System, he is chief of the neurology service and director of the Center for Tissue Regeneration, Repair and Restoration. His research focuses on the development of muscle tissue, the molecular control of muscle stem cell differentiation, the functionality of older muscle stem cells and the molecular basis of muscular dystrophy and potential therapies for it.

Carstensen is a professor psychology, the Fairleigh S. Dickinson Jr. Professor in Public Policy and founding director of the Stanford Center on Longevity. Her research addresses changes in motivation and emotion across adulthood and the ways that these changes influence cognitive processing, decision making and health practices.

Established in 1970, the National Academy of Medicine, formerly called the Institute of Medicine, is recognized as a national resource for independent, scientifically informed analysis and recommendations on health issues. The academy's almost 2,000 active members are selected on the basis of their professional accomplishments and volunteer service. **ISM**

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STANFORD MEDICINE

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 suspect that this test could be used 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 Immunity, 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 thrumming, 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 inflammation, 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 asymptomatic individuals.

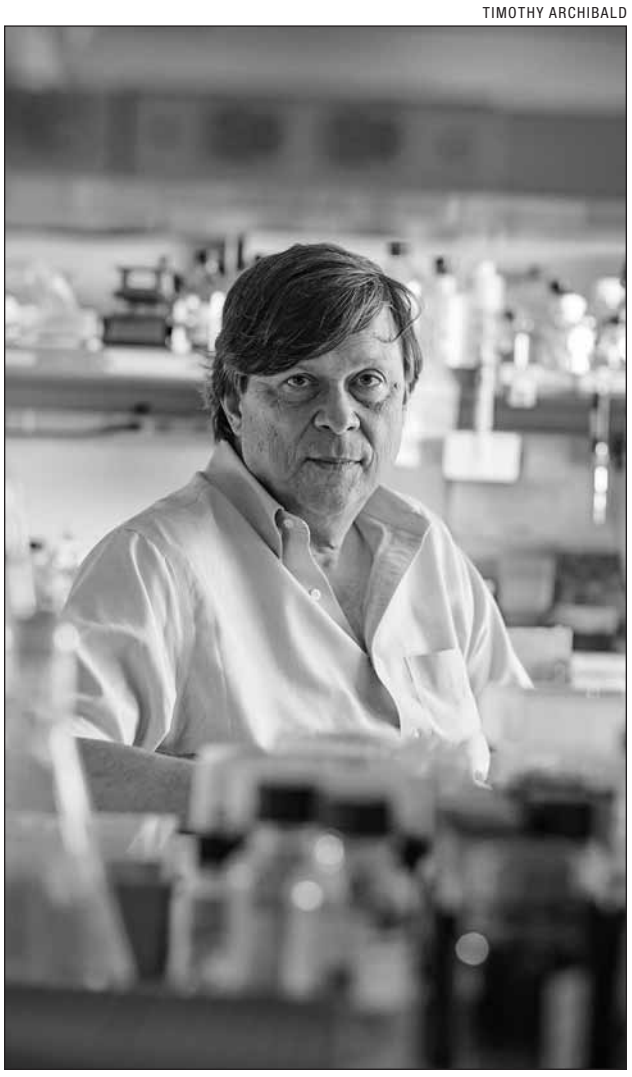
The researchers took advantage of data from the first three years of what was to become a nine-year longitudinal project carried out at Stanford under the direction of study co-author Cornelia Dekker, MD, a professor of pediatric infectious disease. In all, 90 adults, divided into two groups — people younger than 40 and people older than 60 — were assessed annually at high resolution 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 intracellular 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 erstwhile quiescent cell into a frenzy of immunological activity.

TIMOTHY ARCHIBALD



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

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.

The investigators blended 15 separate cytokine-responsiveness measurements to generate a single number called a cytokine response score. This measure, which varied considerably among different older adults, was quite stable from year to year for any given individual. A higher CRS is better, as it indicates a more-responsive immune system and lower background inflammation.

Intriguingly, individuals taking fish-oil supplements had higher scores. (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 Francois Haddad, MD, a clinical associate professor of cardiovascular medicine, the cytokine response score of each of 40 older subjects was then cross-referenced against cardiovascular-health assessments they underwent up to two years later. These assessments included a comprehensive clinical history and tests of atherosclerotic 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 atherosclerosis 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 atherosclerosis and with two measures associated with the heart's ability to relax between beats. Importantly, the borderline subjects also had low 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 expensive. Davis said he and his colleagues want to try to simplify it and drive down the cost.

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

The team's 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 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 Rosenberg-Hasson, PhD, immunoassay and technical director at the Institute for Immunity, Transplantation and Infection; Sally Mackey, associate director of the Stanford-LPCH Vaccine Program; Armaghan Grisar, MD, research fellow at the Stanford Cardiovascular Institute; associate professor of microbiology and immunology Holden Maecker, PhD; professor of microbiology and immunology Yueh-hsiu Chien, PhD; professor of radiology Joseph Wu, MD, PhD; and former associate professor of pediatrics Atul Butte, MD, PhD, now at the University 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 Immunology also supported the work. **ISM**

Two researchers receive funding from BRAIN Initiative

Two School of Medicine researchers are among the recipients of the third round of grants from the National Institutes of Health's BRAIN Initiative.

More than 100 new awards, totaling more than $70 million, are being given this year to over 170 investigators working at 60 institutions. These awards expand 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.

Kim Butts Pauly

Vinod Menon

The two Stanford recipients are Vinod Menon, PhD, professor of psychiatry and behavioral sciences, and Kim Butts Pauly, PhD, professor of radiology.

Menon received $387,000 from the NIH's National Institute of Biomedical Imaging and Bioengineering for a project titled "Novel Bayesian linear dynamical systems-based methods for discovering human brain circuit dynamics in health and disease." He and his colleagues plan to develop novel algorithms for identifying dynamic functional networks in the brain and characterizing network interactions between brain regions involved in cognitive tasks.

Butts Pauly received $393,000 from the NIH's National Institute of Mental Health for a project titled "MR-guided focused ultrasound neuromodulation of deep brain structures." Through the work, she hopes to develop noninvasive technology that combines focused ultrasound neuromodulation for therapeutic purposes with magnetic resonance imaging to accurately predict ultrasound intensities and temperatures at the target site and throughout the brain. **ISM**

Study: Withholding amino acid depletes blood stem cells

By Christopher Vaughan

A dietary approach to depleting blood stem cells may make it possible to conduct bone marrow transplantations 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 way to treat 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 Taya, 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, much lower. 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 also 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 Medicine, has a particular interest in one kind of stem cell that may be affected by valine deficiency. If leukemia stem cells are also vulnerable to valine deficiency, Nakauchi said, it may open the door to a dietary therapy for these blood cancers. As with bone marrow transplantation, a dietary treatment for cancer would probably be much less toxic than chemotherapies now being used, he said.

"This work could open up a new research field of stem cell metabolism."

The lightbulb

The new study came about after Yamazaki was reviewing the scientific literature and found an article in a 1946 issue of *Science*. It was co-authored by the late Stanford researcher Arthur Kornberg, who would go on to receive the 1959 Nobel Prize in Physiology or Medicine. In his 1946 research, Kornberg and his colleagues showed that certain types of anemia in rats could be treated by giving them mixtures of purified amino acids.

Yamazaki, Nakauchi and their colleagues were intrigued and did the experiments that Kornberg did not do: testing the effects of the presence or absence of specific amino acids on blood stem cells. The researchers found that in a lab dish, a lack of valine or another amino acid, cysteine, would make the growth of mouse blood stem cells impossible.

Then, the researchers asked a company to create mouse food that was deficient in only these specific amino acids, and fed the mice this diet for four weeks. They found that the valine-deficient diet, but not the cysteine-deficient diet, depleted blood stem cells in the mice. "Unlike valine, cysteine is not an essential amino acid, which means that the body can make some of it itself," Nakauchi said. "All of our valine has to come from our diet, however."

The current dietary method complements other work recently reported by Stanford scientists for using antibodies instead of chemotherapy or radiotherapy to clear out blood stem cells in preparation for bone marrow transplantation. "The two methods might even be used together to provide an even more effective, gentler therapy," Nakauchi said.

The mechanism by which amino acid deficiency affects blood stem cells is unknown, he said, but that will be the focus of future research. Now that this amino acid has shown promise as the basis for a dietary therapy, Nakauchi thinks scientists may find other specific kinds of stem cells that are affected by the presence or absence of particular amino acids. "This work could open up a new research field of stem cell metabolism and become the basis for a whole range of dietary therapies," he said.

"It also reinforces the importance of a well-rounded diet to keep all our cells healthy," he added.

The other Stanford co-author is postdoctoral scholar Adam Wilkinson, PhD.

This work was supported by the California Institute for Regenerative Medicine, the Siebel Foundation, Ludwig Cancer Research, the Japan Science and Technology Agency, the Japanese Ministry of Education, Culture, Sport, Science and Technology, and the Japan Society for the Promotion of Science.

Stanford's Department of Genetics and the Stanford Institute for Stem Cell Biology and Regenerative Medicine also supported the work. **ISM**

WING HON FILMS

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.

Common prostate cancer treatment linked to later dementia

By Jennie Dusheck

A new retrospective study of patient medical records suggests that men with prostate cancer who are treated with testosterone-lowering drugs are twice as likely to develop dementia within five years as prostate cancer patients whose testosterone levels are not tampered with.

The study, by researchers at the Stanford School of Medicine and the University of Pennsylvania Perelman School of Medicine, also demonstrates emerging techniques for extracting biomedical data from ordinary patient medical records.

The paper describing the research was published online Oct. 13 in *JAMA Oncology*. Kevin Nead, MD, DPhil, a resident at the University of Pennsylvania who got his medical degree at Stanford, is the lead author. Nigam Shah, MBBS, PhD, associate professor of biomedical informatics research at Stanford, is the senior author.

Testosterone can promote the growth of prostate tumors, and so clinicians have used androgen deprivation therapy to lower testosterone and other androgens in prostate cancer patients since the 1940s. In the United States, about a half-million men currently receive ADT as a treatment for prostate cancer.

ALEXANDER RATHS / SHUTTERSTOCK.COM

Nigam Shah

'The risk is real'

A 2015 study by the same authors found an association between ADT and Alzheimer's disease. In the new paper, the team expanded their work to include several other forms of dementia. "When we published our last paper, a letter to the editor pointed out that Alzheimer's is often confused with vascular dementia," said Shah. "So instead of looking for Alzheimer's and dementia separately, we decided to aggregate them into a higher-level category — all dementias and cognitive decline." Such aggregation could minimize the question of misdiagnosis, Shah said, and increase the sample size to provide more statistical power.

The team looked at deidentified records from Stanford Medicine's clinical-research data warehouse for nearly 10,000 patients with prostate cancer. Of the 1,829 who received androgen deprivation therapy, 7.9 percent developed dementia within five years, compared with 3.5 percent of those not treated with ADT.

"The risk is real and, depending on the prior dementia history of the patient, we may want to consider alternative treatment, particularly in light of a recent prospective study from the U.K.," said Shah. That study, published in September in *The New England Journal of Medicine*, revealed that prostate cancer patients randomized to either active monitoring, surgery or radiation therapy all had the same risk of death from the cancer after 10 years. Ninety-nine percent of men in the study survived regardless of initial treatment. These startling results suggest that active monitoring of prostate cancer patients may be as good as early radical treatment and may cause fewer side effects.

And because the actual number of patients possibly at risk for dementia from androgen deprivation therapy is small, it makes sense when weighing the value of prescribing ADT to try to identify which prostate cancer patients might be vulnerable to dementia, said Shah.

The new study adds to a growing body of evidence supporting Stanford Medicine's precision health approach, the goal of which is to anticipate and prevent disease in the healthy and precisely diagnose and treat disease in the ill.

Nead and Shah cautioned that pros-

See PROSTATE, page 5

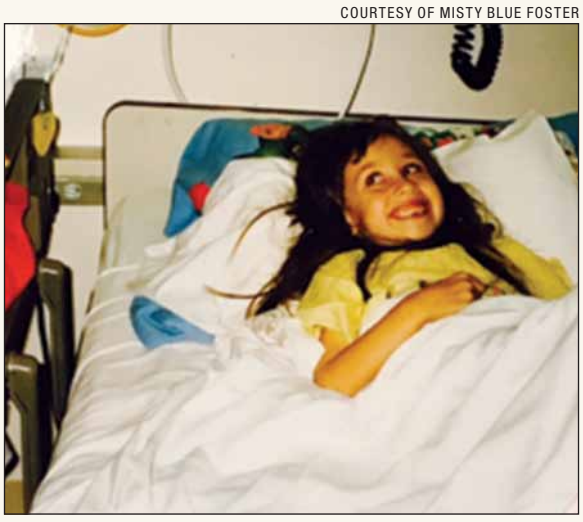
Growing up in a hospital: My 25 years with Packard Children's

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 have until I found myself in the hospital.

COURTESY OF MISTY BLUE FOSTER



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

Finding my voice

Born 3 months premature 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 whirling of the machines for company. This experience taught me to advocate for myself and to ask questions so I 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 Cote, 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."

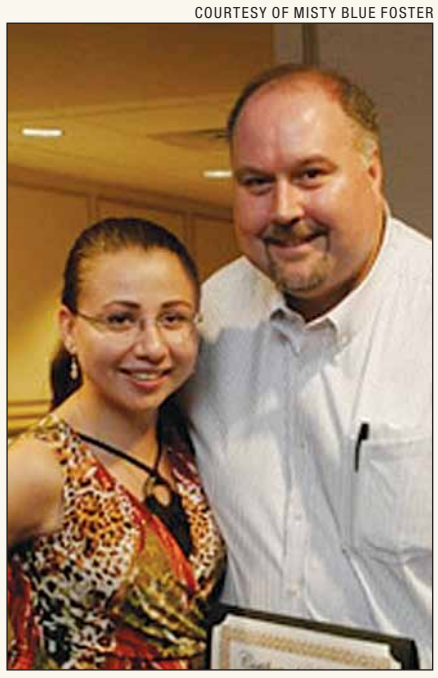
I also have Packard "grandparents." I met Grandpa Dave Olsen when, as a volunteer, he came to read stories to me, something he dedicated himself to after losing his own grandson to cancer. I explained to him that I was alone, and he assured me, "I'll be your grandpa." He kept true to his promise, and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

COURTESY OF MISTY BLUE FOSTER



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

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 clinics, 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 blast injuries, 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. **ISM**

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

COURTESY OF MISTY BLUE FOSTER

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

Prostate

continued from page 4

tate cancer patients who are receiving ADT shouldn't make changes to their medications without talking to their physicians.

Cheaper and faster

"I was surprised at how ubiquitous the effects on all types of dementia were, but I would definitely not alter clinical care based on our results," Nead said. He added that he would like to see a prospective, randomized clinical trial to establish whether ADT can be more firmly linked to an increased risk of dementia and to help identify what kinds of patients might be vulnerable to that increased risk. He anticipates that checking for dementia risk in people treated with ADT will be part of future randomized, clinical trials that have a larger focus.

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, and our current efforts, which are funded by the Dean's Office, have gotten us to close to two to three days."

"I was surprised at how ubiquitous the effects on all types of dementia were."

In contrast, a prospective, randomized clinical trial to study the same question would probably require thousands of patients, years to complete and 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 Mahaffey. "This work is important," he said, "but there are a number of examples of such retrospective studies where the results have been completely wrong."

Shah said the approach his team used minimized the chance of being wrong. For example, the authors matched patients who received ADT and those who did not according to how sick they were. They also explicitly and empirically quantified the chance of being wrong by testing associations they knew were not true, calibrating their approach.

Retrospective studies of patient medical records aren't meant to replace randomized clinical trials, said Shah. "If we had infinite funding, we'd do a trial for everything. But we don't have that," he said. "These cheap, few-week studies can guide us where to point our clinical trial dollars."

Other Stanford-affiliated co-authors are medical student Greg Gaskin; senior scientist Cariad Chester; and associate professor of vascular surgery and of cardiovascular medicine Nicholas Leeper, MD.

This 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. **ISM**

Unroofing

continued from page 1

chest pain and examine them in the catheterization laboratory using diagnostic-imaging techniques, such as angiograms, to visualize the arteries of the heart and its chambers.

"Sometimes we saw myocardial bridging on the angiogram," she said. "Then we'd use an intravascular ultrasound to see them more clearly."

Since then, 150 participants in this ongoing study have been diagnosed with myocardial bridges. Research has involved measuring blood flow and blood pressure in the bridging vessel. Schnittger and her colleagues were able to show that compression of the heart muscle can reduce or cut off blood flow in the artery, resulting in serious problems, including angina, myocardial ischemia, acute coronary syndrome, left ventricular dysfunction and malignant ventricular arrhythmias.

For some, symptoms are severe

"It hadn't before been proven with blood-flow studies that circulation got impaired enough to cause ischemia, inadequate blood flow and oxygen to the heart muscle," Schnittger said.

Most patients with the condition remain asymptomatic. Some have minor symptoms that can be controlled with medication, such as beta blockers and calcium-channel blockers.

But a small portion have severe symptoms that greatly affect their daily lives. Some are left homebound. Many make repeated trips to emergency rooms complaining of heart-attacklike symptoms, only to get sent home with no answers.

> "Many of these patients have these heartbreaking stories to tell."

"Many of these patients have these heartbreaking stories to tell," Schnittger said. "They can't hold a job, they can't travel, they can't take care of their families. Most cardiologists are completely at a loss. They know myocardial bridges exist, but they have been taught they are benign and never cause problems.

"When these patients go to the ER, and they go there a lot, all the cardiology tests come back normal. They're told, 'Here's a little Valium. I think you're anxious.' 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 artery, thus relieving compression on the artery caused by the bridging.

The surgery is known to be effective, Boyd said. However, concerns that healthy heart muscle could be damaged during the operation have slowed its adoption. "At Stanford, we use new imaging techniques to map the bridge muscle very precisely, and we perform the unroofing with conservative surgical techniques to safeguard the healthy heart muscle," he said.

Ingela Schnittger

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 Jennifer 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 Stanford in the past five years.

For the new study, the researchers 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 using a heart-lung machine for life support. The last 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 Seattle angina questionnaire, a three-page survey describing 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 frequently they have it, how much it limits their life.

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

"Our patients come back after surgery so grateful," Schnittger said. "They have suffered for so long — finally they've found doctors who understand them.

"One patient, a mother of five, was so symptomatic before surgery she had arranged her whole life around her symptoms. 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 established at Stanford Health Care.

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 postdoctoral scholar Vedant Pargaonkar, MD; resident David Scoville, MD; Takumi Kimura, MD, PhD, Shigemitsu Tanaka, MD, PhD, and Ryotaro Yamada, MD, PhD, all members of the Stanford University Cardiovascular Core Analysis Laboratory; Michael Fischbein, MD, PhD, associate professor of cardiothoracic surgery; and R. Scott Mitchell, MD, professor emeritus of cardiothoracic surgery.

Stanford's departments of Medicine and of Cardiothoracic Surgery supported the work. ISM

■ OBITUARY

Radiologist, pianist F. Graham Sommer dies at 70

By Jennie Dusheck

Frank Graham Sommer, MD, a professor emeritus of radiology at the School of Medicine and an accomplished pianist, died Oct. 2 of amyotrophic lateral sclerosis at his home on the Stanford campus. He was 70.

An expert in ultrasound imaging and other radiological imaging techniques, Sommer received the 2016 Academy of Radiology Research's Distinguished Investigator Award. His genial personality helped create a warm, collegial and 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, British Columbia, in 1946. He earned a bachelor's degree in physics from the University of Victoria and a medical degree from McGill University in Montreal. He joined the faculty at Stanford in 1979.

COURTESY OF MCGILL UNIVERSITY

An expert in ultrasound imaging and other radiological imaging techniques, F. Graham Sommer was also an accomplished pianist and would perform at restaurants and senior centers.

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 stereotype of the super-focused, socially inept scientist, she said. Sommer was adventurous, thoughtful, kind, generous and charming, she said. He was also very logical and a careful planner, 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 Filoli, an estate in Woodside that's open to the public, and at restaurants and senior centers — favoring classical, popular and ragtime music.

Sommer recently pledged $1 million to McGill University to fund a Canada-wide competition for composers. The competition, intended to support composers under age 35 and to promote the creation of new musical works, will launch 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 playing 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 everything he did carefully, carrying his research habits into his daily life. In 1995, when Sommer and Leclair had just 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 decided to throw some blackberries inside the filo dough with the salmon. "He was astounded!" Leclair laughed. And he never forgot that she had done that, often bringing it up in later years.

In addition to Leclair, Sommer is survived by a sister, Anne Axford, 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 Arastradero Road, Palo Alto. ISM

Antidepressants

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MRI 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."

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 predict how the individual patients would respond immediately after the eighth week. "Our predictions were correct," Goldstein-Piekarski said.

Using a statistical analysis called predictive modeling, study results showed that participants exposed to a high level of childhood trauma were most likely to recover with antidepressants if the amygdala was reactive to the happy faces. Those with a high level 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."

"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, they have 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 negative and positive emotions coming from that person in order to avoid future adverse events, Goldstein-Piekarski said. As a result, the amygdala becomes hypersensitive to these emotions. And that's useful at that time.

"Unfortunately, sometimes the amygdala maintains this hypersensitive trajectory 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 brain" — the network or circuit of the brain that responds to emotions — 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 integrated clinic of the future 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 a trial-and-error period 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.

Stanford's Department of Psychiatry and Behavioral Sciences also supported the work. ISM

LESLIE WILLIAMSON

Leanne Williams and her colleagues say that using functional MRI scans and a questionnaire can help predict which patients are likely to be helped by antidepressants.

Hadron

continued from page 1

Unlike photons or electrons, which release energy along the length 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 inside of 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. If all goes well, the collaborators hope to begin treating cancer patients in about four years.

"Hadron therapy represents a new way forward in cancer care," said David Entwistle, president and CEO of Stanford Health Care. "Stanford Medicine is honored to collaborate with the VAPAHCS to bring this therapy to our patients, giving them unprecedented access to the latest cancer science and treatment."

VA Secretary Robert McDonald said, "We are excited to further expand our current partnership with Stanford Medicine and explore ways to continue taking veterans' health care into the 21st century. The state-of-the-art hadron center would not only improve the lives of those affected by cancer, but further demonstrate VA's ability to partner on pioneering innovation and exceptional health care."

Goal of improving survival rates

The technology could bring hope to patients suffering from currently incurable tumors.

"Currently it is not possible to effectively treat large-volume tumors or metastatic disease with conventional radiotherapy due to concerns about toxicity," said Quynh Le, MD, professor and chair of radiation oncology at the School of Medicine and the Katharine Dexter McCormick & Stanley McCormick Memorial Professor. "I believe particle beam therapy will transform the care of cancer in this country. We will have the potential to cure patients with 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 currently 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 pediatric 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 particle 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 Sridhar Seshadri, 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." ISM

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 population 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's historically been fantastic at Stanford, which is the laboratory sciences, and to recognize that in fact without quantitative science we will never be a great science institution. That culture shift would represent a real sea change."

He said he also hopes to spur the "development of true team science," in which researchers from diverse disciplines inside and outside the medical school work together on complex problems that impact human health and longevity.

Mark Cullen

"I'm talking about building groups that include, for instance, geneticists and sociologists and clinical scientists and engineers — people whose fundamental way of asking questions is different," he said. "If we are going to answer questions like, 'What happens after the moment of conception that changes your chance of getting disease or being healthy?' we will need many disciplines. Without such diverse teams, we will never understand how social networks do or don't contribute to our health. We will not understand how living in a complex, urban environment impacts the way people survive, or why and how they develop chronic disease and what we might do to change that. These are questions that require many intellectual inputs."

Big data pioneer

Cullen has been a pioneer in big data; long before the practice became popular, he was using large collections of data to study human health. In the late 1990s, while at Yale University, he began a longstanding relationship with Alcoa, America's largest aluminum producer, in which he and his colleagues from various fields assembled health, environmental and other records to study the environmental and psychosocial causes of disease in the workforce. In the process, they began to understand many issues, such as how early life impacts the risk of disease later in life, and how a person's health may be affected by major life changes, such as financial setback. The work contributed to important occupational health reforms and helped validate the field of data science.

Cullen and Greenberg will serve as co-principal investigators for the school's research activities as part of the National Institutes of Health's Clinical and Translational Science Award consortium until May 2017. Cullen will serve as the sole lead investigator following the grant's renewal.

In announcing the appointment, Minor also praised Greenberg, a professor of medicine and specialist in viruses affecting the gastrointestinal tract, liver and respiratory system. He has had led the school's research enterprise since 2002.

"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." ISM

Sylvester named an associate dean for maternal and child health

By Erin Digitale

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

Karl Sylvester

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. 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-senior associate deans for research Mark Cullen, MD, and Harry Greenberg, MD, Sylvester will focus on aligning the pediatric 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.

He will emphasize building on the existing infrastructure of Spectrum Child Health and ensuring an efficient collaboration with colleagues and stakeholders at Stanford Health Care and the medical school.

"Karl will assist in developing the necessary infrastructure resources to facilitate translational and clinical research in Lucile Packard Children's Hospital Stanford for all pediatric investigators across the School of Medicine and university," Stevenson said.

Sylvester is also medical director of Packard Children's Pediatric Trauma Program, and since 2013 he has been executive director of the hospital's Program for Fetal and Maternal 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 diagnostics of newborn diseases, such as necrotizing enterocolitis and sepsis. He is widely published on the clinical care of necrotizing enterocolitis 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. ISM

OF NOTE

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

TANDY AYE, MD, was promoted to associate professor of pediatrics, effective Aug. 1. She is a pediatric endocrinologist whose research and clinical work focuses on how blood glucose values and sex hormones affect children's brains.

ALISTAIR BOETTIGER, PhD, was appointed assistant professor of developmental biology, effective Sept. 1. His research uses single-molecule microscopy to understand how noncoding sequences in the genome interact physically to shape genome structure and regulate gene expression.

JOACHIM HALLMAYER, MD, was promoted to professor of psychiatry and behavioral sciences, effective July 1. His research focuses on the genetics of autism and narcolepsy, as well as on the genetics of disorders such as 22q11 deletion syndrome and Turner syndrome that can cause neuropsychiatric problems.

RAMASAMY PAULMURUGAN, PhD, was promoted to associate professor (research) of radiology, effective Aug. 1. His research focuses on developing new therapies for triple-negative breast cancer, a form of cancer that lacks three types of receptors and has no targeted therapies available for treatment.

NATALIE RASGON, MD, PhD, professor of psychiatry and behavioral sciences, has received a Sex and Gender in Alzheimer's Disease grant from the Alzheimer's Association. The grant provides $250,000 over three years. She will investigate whether there are sex differences in the way risk factors interact to affect the development of Alzheimer's disease.

JOSEF RUZEK, PhD, was appointed professor of psychiatry and behavioral sciences, effective June 1. He directs the Dissemination and Training Division of the U.S. Department of Veterans Affairs National Center for Post-Traumatic Stress Disorder .

CHIARA SABATTI, PhD, was promoted to professor of biomedical data science and of statistics, effective Aug. 1. She develops statistical methods to uncover the molecular basis of disease, using large heterogeneous data sets.

DAVID K. STEVENSON, MD, the Harold K. Faber Professor of Pediatrics and senior associate dean for maternal and child health, will receive the 2017 Frank H. Morriss Jr. Leadership Award from the University of Iowa Carver College of Medicine. The honor, given to two researchers in 2017, recognizes academic leadership that has improved the well-being of children. Stevenson will travel to Iowa to accept the award in April. He is a neonatologist who specializes in neonatal jaundice and the prevention of preterm birth.

CHI-HO BAN TSUI, MD, was appointed professor of anesthesiology, perioperative and pain medicine, effective Aug. 1. ISM

Tandy Aye

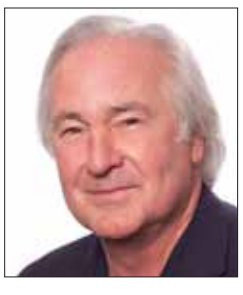
Alistair Boettiger

Joachim Hallmayer

Ramasamy Paulmurugan

Natalie Rasgon

Chiara Sabatti



David K. Stevenson