Stanford Hospital is first in nation to earn comprehensive stroke center designation

By Sara Wykes

Stanford Hospital & Clinics is the first hospital in the country to earn the newest level of certification for advanced stroke care, awarded by the Joint Commission, the nation's oldest and largest standards-setting and accrediting body in health care.

"Stroke patients who are treated at Stanford can have confidence that the hospital has put in place the critical elements necessary to meet their unique needs," said commission president Mark Chassin, MD, in announcing the certification on Nov. 16. "The Joint Commission commends Stanford Hospital & Clinics for seeking and achieving certification as part of its commitment to focusing on the care processes that produce the best outcomes for complex stroke patients.

A team of Joint Commission expert surveyors evaluated Stanford Hospital & Clinics and its Stroke Center for two days in October for its compliance with the new comprehensive stroke center standards and requirements, including advanced imaging and treatment capabilities, 24/7 availability of specialized treatments, participation in research, and staff with the unique education and competencies to care for complex stroke patients. The surveyors found the hospital met or exceeded all required standards.

"We are very pleased to have earned the Joint Commission and the American Heart Association/American Stroke Association's recognition. The leading-edge standards of care the Stanford Stroke Center team developed and refined over the last 20 years should be upheld as a national model," said Amir Dan Rubin, president and CEO of Stanford Hospital & Clinics.

Rubin added that the center's founders "knew from the very start that the most effective way to battle complex stroke cases was to create a truly coordinated, multidisciplinary team that united experts from every related field — not just those dedicated to neurology, neurosurgery and interventional neuroradiology, but also experts in nursing, rehabilitation, emergency medicine and pharmacy, amongst others. This approach has improved patient outcomes and pioneered significant advances in stroke diagnosis and treatment."

Nearly 1 million people in the United States were hospitalized by stroke in 2009, according to the Centers for Disease Control and Prevention. An estimated 7 million Americans have had some form of stroke. It was the fourth-leading cause of death.

Back in the Bay Area: Sabbatical draws stem cell expert Pedersen to Stanford

By Christopher Vaughan

Roger Pedersen — the stem cell researcher who famously left UC-San Francisco in 2001, citing an increasingly unfriendly climate for stem cell research in the United States — has come to Stanford's Institute for Stem Cell Biology and Regenerative Medicine for a one-year sabbatical.

Pedersen's 2001 departure for the U.K., and the reasons for it, became part of a clarion call for greater non-federal support for stem cell research. That move, and the establishment of Proposition 71 and the California Institute for Regenerative Medicine, culminated in 2004 with the passage of Proposition 71 and the establishment of the California Institute for Regenerative Medicine.

While at Stanford as a Siebel Scholar, Pedersen will conduct research, teach and collaborate with other researchers as part of his leave from the University of Cambridge, where he is director of research in the Anne McLaren Laboratory for Regenerative Medicine.

Pedersen transferred his research from UCSF to Cambridge just over a decade ago as the U.S. government was clamping down on federal funding for embryonic stem cell research. Although Pedersen actually decided to leave before then-President George W. Bush announced a controversial policy that limited federal funding for embryonic stem cell research to a small number of existing cell lines, there was already a ban on federal funding for research on human embryos. Pedersen and UCSF halted some research in his lab because ambiguities over National Institutes of Health policies made it unclear whether federal funding of overhead costs required that even non-federally funded embryo research be done "off campus."

In the fall of 2000, Pedersen had taken a short sabbatical at Cambridge, which gave him the chance to observe the U.K.'s parliamentary debate over embryonic stem cell research. "It went the opposite way to our debate," he said, of the British lawmakers' decision to allow all human embryo research "for treatment of serious diseases."

Pedersen told one of the debaters, Cambridge's Clinical School head, Sir Keith Peters, to let him know if there was anything he could do to help, to which Peters replied, "You could come here."

School groups move to Porter Drive site

By Ruthann Richter

Some 1,200 to 1,300 School of Medicine faculty and staff are in the process of establishing new homes on Porter Drive in Palo Alto, a cluster of seven buildings located south of the main campus.

Administrative and research employees from the medical school will join a group of university staff already on the site, which is located about 2.5 miles from the main campus. By combining employees from diverse locations and backgrounds in one spot, the university aims to create a whole new community, with services, amenities and activities designed to encourage people to interact in the new shared space.

"We believe this is a momentous time for us," said Niraj Dangoria, the medical school's associate dean for facilities planning and management. "This is the first time we have purposely created an opportunity to co-locate these off-campus outposts. In bringing them together, we have many benefits. We are really creating a community."

With several of its off-campus leases expiring, the School of Medicine began to look to Porter Drive a few years ago, where the university had already begun to establish a presence, he said. Buildings at the site are now occupied by staff from Land, Buildings and Real Estate, the Office of Development,
Making earlier diagnoses when memories begin to fade

By Sara Wykes

Susan Harrel's daughter, Claire, can't list specific moments when her mother, a long-time human resources executive, had early signs of Alzheimer's disease. "I could tell you a million stories about when I was 3 years old, but if I told you I was going to do something, she'd ask me five minutes later if I was going to do something," she said.

Many of her friends' mothers were about the same age, she said, "and they would have said the same thing, 5,000 times. 'That's why I didn't think anything was too different.'"

Harrel's husband, Dave Baker, became concerned when he saw that his highly intelligent wife wasn't just asking him the kind of computer questions that all non-technical folks ask; instead, she was posing questions about content. Her emotions around her work had altered, too. "She'd been a very confident, capable individual and she was becoming more anxious and upset and worried," he said. "She'd started to become obvious that something was changing."

Baker was like many people who notice such differences, and begin to look for answers, especially as advancing age begins to interfere with the dozens of daily tasks once you thought for granted. In the United States, more than 40 million people are over 65 years old; another 80 million are ages 45-64. Of all the diseases related to dementia, more than 10 million are the most feared — a condition that attacks the core of all those qualities that distinguish one person from another and erodes those memories.

Dementia can take many forms; Alzheimer's disease — characterized by the loss of memory and the inability to focus — is the most common, and the most feared.

The Alzheimer's Association estimated that in 2011 5.4 million Americans — about one in eight of those 65 or older — were living with its consequences. Researchers have yet to understand what triggers the imbalance in brain chemistry that degrades its normal function, shrinking its overall size, and depositing tangles and plaques that block the millions of daily neuronal interactions.

Progress has been made, however, in diagnosing diseases of the brain. Until recently, physicians were left only autopsies for definitive diagnosis.

Now, at facilities like Stanford Hospital & Clinics Center for Memory Disorders, where Harrel was asked to seek care, patients have new options that, in combination with additional tests, provide a much earlier sense of direction.

Looking for answers

"My job is to try and figure out first if there's anything we can fix right away," said Geoffrey Kerchner, MD, PhD, a Stanford behavioral neurologist who became Harrel's doctor. "When a patient comes to me with a complaint about memory, my approach is like that of any physican — I have to understand what medicines they're on, what their thyroid function and vitamin B12 levels are — to try to discover what the cause could be."

Harrel's tests included an MRI to look for signs of a stroke or other brain injury. All came back with no obvious cause for her cognitive struggle. The next step, Kerchner said, was objective neuropsychological assessment, a set of tests that solve the dilemma for many who wonder if their memory lapses are something to worry about. The assessments focus on the cognitive and behavioral changes that occur with the onset of memory injury, cerebrovascular disease, multiple sclerosis, dementia, brain tumor, Parkinson's disease, epilepsy and attention deficit/hyperactivity.

"When we look at behavior and the brain, we find there's a complex inner relationship," said Stanford psychologist Gayle Deutsch, PhD. "A lot of our behaviors become automatic over our lifetime, but when we break them apart, there is a great deal of complexity."

Deutsch began the process of ascertaining Harrel's problems truly began. That territory includes intellectual and executive function, language skills, visual-spatial abilities, attention, memory, motor skills and mood. Deutsch begins with a set of tests to distinguish those changes that emerge with normal aging and those linked to neurodegenerative conditions.

She will also engage a family's friends and for their observations. "Our tests are good at measuring con- ceptual reasoning and problem solving," Deutsch said, but they're also important to look at everyday behavior. Are people showing social skills appropriate for their age? Sometimes people with certain kinds of dementia may seem less capable of reading social cues. Or they may become apathetic and show no interest in the world around them. Today we're looking for abnormalities that are caused by the disease itself," Kerchner said, "so it can provide positive evidence of the disease."

A second test, just approved by the FDA, uses radioactive particles that seek out and mark amyloid plaques in the brain. Those two tests, he said, are so helpful to Alzheimer's that, for select patients, they may reduce the need for other tests.

"Finally came the moment when, as Harrel remembers it, Kerchner 'got nose to nose with me,' and told her that she had early onset Alzheimer's. She was 59," Baker said. "I was surprised. I was in denial. I thought the whole party was over — work and everything. I can't work. I can't drive. It was like everything was going past me."

"It's hard," Baker said, "We did a lot of crying and mourning and a lot of being upset. We've moved through that now and we're just looking for the positive sides, so today I can help other people going through this disease, how Susan can help with research and how we can just enjoy ourselves in our day."

Finding peace

Being diagnosed with Alzheimer's is "a big hit," Kerchner said, "but by the time a patient has a physician tell them, 'I think you have Alzheimer's disease,' it may be too late to find some- thing thing's going on with their brain. They know it and they're worried. Having an answer helps a patient who is unclear about their prognosis and what's likely to happen in the coming years. I think people achieve a lot of peace in mind in having a name on what they have and in being acknowledged by the medical community."

"Having a garden and a dog is really healthy if you're going through something like this," Harrel said. "I paint. I have things to do. I have great friends. My job right now is to go to Stanford and do what I need to do with Dr. Kerchner, to be there for someone, to have conversations. It's good to connect with someone else who's going through what you are so you don't feel like, 'Oh, it's just me.' I'm the purple goose going down the street. I want to get it out and talk about it — to be a waving flag for Alzheimer's and for Stanford."

The garden in particular gives her a sense of purpose and reward. "I see the color every day and I'm like, 'Life is beautiful.' I know there's a lot more in our future around this, too," Baker said. "Every day we just get up and do the best we can, and where we end up is in some- body else's hands." Baker was diagnosed with heart failure several years ago, and his condition has been stabilized. "There were some moments in therapy and I'm still around," he said. "We're really hoping the same thing can happen for Susan's disease — and that at least we get there for all the people who have Alzheimer's as well."

Sara Wykes is a writer for the Stanford Hospital & Clinics communications office.

Participants sought for experimental flu vaccine trial

By Rosanne Spector

Researchers at the School of Medicine are recruiting participants for a clinical trial of a new vaccine. The new vaccine is an experimental, seasonal DNA flu vaccine and boosted by one of two licensed seasonal flu vaccines, which are given either into the skin or into the muscle of the upper arm.

The trial's immediate goals are to test the safety of the experimental DNA vaccine, given alone or at the same time as the licensed vaccines, and to assess the immune responses they produce. The ultimate goal of the trial, sponsored by the National Institutes of Health, is to learn more about how to safely improve the immune response to seasonal flu vaccines.

"Currently available flu vaccines are good but they leave room for improvement and for them they've been given every year before the new flu season," said Cornelia Dekker, MD, PhD, a professor of pediatrics and medical director of the Stanford-LCPH Vaccine Trial Program. "The hope for influenza researchers would be a vaccine that covers all potential strains, including future pandemic ones, with just one injection."

"Every so often, a new type of influenza virus evolves that is different enough from past viruses that the population does not have immunity. In this situation, called a pandemic influenza, the virus rapidly spreads around the world. The pandemic in 1918 is esti- mated to have killed 50 million people. A successful universal influenza vaccine might help us avoid such a global disaster," Dekker said.

Currently approved seasonal flu vac- cines are made using either inactivated virus given as an injection, or weakened live virus given as a nasal spray. The DNA vaccine is a new ap- proach, using DNA that has been genetically engineered to produce a single, specific protein from each of the three types of influenza virus types included in the vaccine formulation. The DNA is injected using a needle- free device into the muscle of the upper arm, where the cell's genetic machinery follows the DNA instructions to make the virus proteins. The

Inside Stanford Medicine is published monthly in July and December and semi-monthly the rest of the year.

Paul Costello
Office of Communication & Public Affairs
Susan Ipaktchian
Director of print & web communications
Robin Weiss
Graphic designer

Inside Stanford Medicine is currently approved seasonal flu vac- cines are made using either inactivated virus given as an injection, or weakened live virus given as a nasal spray. The DNA vaccine is a new ap- proach, using DNA that has been genetically engineered to produce a single, specific protein from each of the three types of influenza virus types included in the vaccine formulation. The DNA is injected using a needle- free device into the muscle of the upper arm, where the cell's genetic machinery follows the DNA instructions to make the virus proteins. The

Inside Stanford Medicine is published monthly in July and December and semi-monthly the rest of the year.

Paul Costello
Office of Communication & Public Affairs
Susan Ipaktchian
Director of print & web communications
Robin Weiss
Graphic designer


Send letters, comments and story ideas to Susan Ipaktchian at 725-5375 or at susan@stanford.edu. Please also contact her to receive an e-mail version of Inside Stanford Medicine.

Currently approved seasonal flu vac- cines are made using either inactivated virus given as an injection, or weakened live virus given as a nasal spray. The DNA vaccine is a new ap- proach, using DNA that has been genetically engineered to produce a single, specific protein from each of the three types of influenza virus types included in the vaccine formulation. The DNA is injected using a needle- free device into the muscle of the upper arm, where the cell's genetic machinery follows the DNA instructions to make the virus proteins. The


Send letters, comments and story ideas to Susan Ipaktchian at 725-5375 or at susan@stanford.edu. Please also contact her to receive an e-mail version of Inside Stanford Medicine.

Currently approved seasonal flu vac- cines are made using either inactivated virus given as an injection, or weakened live virus given as a nasal spray. The DNA vaccine is a new ap- proach, using DNA that has been genetically engineered to produce a single, specific protein from each of the three types of influenza virus types included in the vaccine formulation. The DNA is injected using a needle- free device into the muscle of the upper arm, where the cell's genetic machinery follows the DNA instructions to make the virus proteins. The


Send letters, comments and story ideas to Susan Ipaktchian at 725-5375 or at susan@stanford.edu. Please also contact her to receive an e-mail version of Inside Stanford Medicine.
New study calms fears about genomic instability of iPS cells

By Bruce Goldman

School of Medicine scientists have demonstrated in a study conducted jointly with researchers at Yale University that human induced-pluripotent stem cells (iPS cells) do not suffer from what previously appeared to be serious genomic instability. The team reports their findings today, "heart cells" derived from a heart patient's own cells may help researchers learn more about that particular patient's condition and the diseases that may arise from the necessity of obtaining embryonic stem cells.

"Concerns arising from the necessity of obtaining embryonic stem cells to study disease or, someday, for regenerative medicine have led to the development of "iPS cells," which are similar to embryonic stem cells from fertilized eggs. iPS cells can be derived relatively easily from a patient's skin, allowing researchers to model genetic variations among the cells comprising our bodies.

That's good news for researchers hoping to use the cells to study disease or learn about the behavior and interactions of various cell types. But iPS cells can be derived easily and quickly from a patient's skin, alleviating ethical concerns from the necessity of obtaining embryonic stem cells from fertilized eggs.

Researchers had been concerned that iPS cells' genetic makeup closely reflects that of the individual from whom they were derived. Today, "heart cells" derived from a heart patient's own iPS cells could help researchers learn more about that particular patient's condition and the diseases that may arise from the necessity of obtaining embryonic stem cells.

However, Urban said, several previous studies have raised worries regarding iPS cells' genomic stability. Whether it was the reprogramming procedure researchers used to convert ordinary adult cells into iPS cells or the culturing techniques employed to keep them alive and thriving afterward, something appeared to be in flux in these new cells. "change in the genome structure that's not consistent from one to the next," Urban said. (Similar concerns apply to embryonic stem cells.)

To see how serious a problem CNVs might pose for iPS cells' use, the collaborators performed tiny skin biopsies on seven volunteers and extracted cells called fibroblasts, which abound in skin and are amenable to cell culture in general and iPS cell generation in particular. From these cells, the team produced 20 separate iPS cell lines in culture. Using now-standard lab methods, the investigators determined, chemical unit by chemical unit, the full DNA sequence of the cells composing each new iPS cell line.

Urban and his colleagues, who had likewise assessed the fibroblasts from which the lines were derived, compared their genetic makeup to that of the cells used to generate iPS cells. The scientists were able to pinpoint numerous CNVs in the new cells that hadn't shown up in the original fibroblasts. CNVs are genomically identical copies of chromosomal segments that reside in only a minority of cells within a tissue. This raised the possibility that the replication of CNVs may be a general characteristic of iPS cells.

"this is a huge amount of cell-to-cell genetic variation," Urban said. "If you did a proteomic analysis, you'd find that out in principle, iPS cells' genetic makeup closely reflects that of the individual from whom they were derived. Today, "heart cells" derived from a heart patient's own iPS cells could help researchers learn more about that particular patient's condition and the diseases that may arise from the necessity of obtaining embryonic stem cells.

"we're just starting to learn what's in these new cells," Urban said. "iPS cell lines sported at least one CNV unshared with either the victim's or the proverbial sore thumb. Six out of the 20 different iPS cell lines in the study of human tissues conducted by the laboratory of Michael Haney, a research technician in the Urban lab, and several Yale investigators co-authored the study, "this reflects differences in parental fibroblasts, it means that CNVs are not monoliths, our bodies may be mosaics composed of cells whose genomes differ when we do not know this, these differences are dangerous, irrelevant or beneficial." But that may depend on the organ, said Urban. "The more complicated something is, the more ways there are that something could go wrong with it. The brain is a particularly complicated organ. CNVs affecting cells in particular brain structures or areas could be playing a key role in psychiatric and neurological disorders such as schizophrenia and autism."

Michael Haney, a research technician in the Urban lab, and several Yale investigators co-authored the study, which was funded by the National Institute of Mental Health, the Simons Foundation and the Stanford University School of Medicine.

Stroke continued from page 1

dead in the United States in 2010.

The new comprehensive stroke center certification was developed by the commission in collaboration with the AHA/ASA and derived from a graded evaluation of nearly 40 years of published data on clinical trials, care and scientific guidelines, research reports on diagnostic and therapeutic approaches to stroke care. The group also sought input from professional organizations.

In 2004, Stanford's Stroke Center earned the Joint Commission's first stroke center certification. "we saw a lot of interest in a common goal, taking care of patients by using what is best from their individual areas of expertise," said David Steinberg, MD, PhD, director of the Joint Commission-certified Stroke Center. "this is part of the center's concept of care, and one particularly commended by the Joint commission surveyors, is the outreach to the community has been a major source of genetic differences between people. CNVs may account for up to several percent of the entire human genome, making them a major source of genetic differences between people. CNVs may account for up to several percent of the human genome.

"we're just starting to learn what's in these new cells," Urban said. "iPS cell lines sported at least one CNV unshared with either the victim's or the proverbial sore thumb. Six out of the 20 different iPS cell lines in the study of human tissues conducted by the laboratory of Michael Haney, a research technician in the Urban lab, and several Yale investigators co-authored the study, "this reflects differences in parental fibroblasts, it means that CNVs are not monoliths, our bodies may be mosaics composed of cells whose genomes differ when we do not know this, these differences are dangerous, irrelevant or beneficial." But that may depend on the organ, said Urban. "The more complicated something is, the more ways there are that something could go wrong with it. The brain is a particularly complicated organ. CNVs affecting cells in particular brain structures or areas could be playing a key role in psychiatric and neurological disorders such as schizophrenia and autism."

Michael Haney, a research technician in the Urban lab, and several Yale investigators co-authored the study, which was funded by the National Institute of Mental Health, the Simons Foundation and the Stanford University School of Medicine.

Correction

A story in the Nov. 5 issue about facemask design named to endowed professors misstated the date one of the professors was awarded a fellowship. D.H. Chen Professorship was created in June by the D.H. Chen Founder's Fund, which was endowed by the late Din-lwa Chen, a Hong Kong-based industrialist and philanthropist.
In the prefrontal cortex that signal motivation. The researchers first introduced their light-sensitive protein into cells in the prefrontal cortex. The light sensitivity then spread out like the branches of a tree through all the outgoing connections and eventually made its way to the brain stem, making those regions light sensitive, too.

Then, illuminating the newly light-sensitive regions of the brain stem thought to control motivational movement, Deisseroth and Warden watched the behavioral effects as a subgroup of neurons in the prefrontal cortex that sent connections to the brain stem were activated. They could see not only which cells are possibly involved in motivation, but the way motivation moves from one brain region to another.

**Mapping motivation**

The researchers suspected that one part of the brain stem in particular, the dorsal raphe nucleus, might be crucial to behaviors that control effort. This cluster of cells is a production hub for serotonin — a chemical messenger that changes mood and behavior. Serotonin is associated with mood modulation, many antidepressant drugs, for instance, may act by increasing serotonin concentration in the brain.

When the pathway between the prefrontal cortex and the dorsal raphe nucleus was stimulated, rodents facing a challenge in the lab showed an immediate and dramatic surge in motivation.

Curiously, when the rodents were relaxing in their home environment, the same stimulation had no effect. The pathway was not merely linked to any action, or to agitation; it was, more specifically, helping to "set the effort that the organism was willing to put forth to meet a challenge," Deisseroth said.

Researchers were also able to produce the opposite effect — reduced effort in response to challenge — by stimulating prefrontal neurons that project to the lateral habenula, a region perched atop the brain stem that is thought to play a role in depression. When this region was getting signals driven optogenetically from the prefrontal cortex, rodents put forward less effort.

**Larger puzzles**

These findings are part of a larger puzzle that Deisseroth and his team have pieced together by using optogenetics to model human behavior in animal subjects. The work has already helped clinicians and researchers to better understand what is going on in a patient's brain.

Connecting depressive symptoms with brain pathways may be helpful in the development of drugs, but according to Deisseroth, the most important part of this research is its insight into how motivation works in both depressed and healthy people.

He has observed that this insight alone can be helpful to those dealing with mental illness and seeking an explanation for troubling symptoms that feel deeply personal. For those patients, he said, simply knowing that a biological reality underlies their experience can be a motivational force in itself.

Other Stanford co-authors include graduate students Ashlan Selimbeysoglu and Sung-Yun Kim; research assistant Julie Mirzabezd; lab manager Maxie Lee; postdoctoral scholars Kimberly Thompson, PhD, and Avishke Adhikari, PhD; and former postdoctoral scholar Kay Tye. They also collaborated with Loren Frank, PhD, a faculty member at UC San Francisco.

This research was supported by the Wiener Family Fund, the Brain & Behavior Research Foundation, a Stanford graduate fellowship, a Samsung scholarship, a Berry Foundation fellowship, the National Institute of Mental Health, the National Institutes of Defense, the Keck Foundation, the McKnight Foundation, the Yu, Snyder, Tarlton, and Woo Foundations, and the Gatsby Charitable Foundation.

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

Keli Servick is a science-writing intern for the School of Engineering's communications office.
Creating light-based ‘remote control’ for proteins inside cells

By Erin Digitale

Stanford scientists have developed an intracellular remote control: a simple way to activate and track proteins using beams of light. The researchers used the method, described in a paper published Nov. 9 in Science, to let researchers shine light on a specific cell region to quickly activate a protein, producing a fine-grained view of the location and timing of protein activity. In addition, the method may eventually enable physicians to direct the movement and function of cells used to treat disease in light-accessible body parts, such as the eye or skin.

The method involves splicing two pieces of a specific fluorescent protein to other proteins of interest. The resulting hybrids — called fluorescent, light- inducible proteins, or FLIPs — have two interesting features: Not only are they turned on by light, but they also glow less brightly when activated, a change that exposes the protein’s active site so it could work.

It’s easiest to build FLIPs from proteins that fold with both their head and tail ends near the active site, though the research team is now figuring out how to attach FLIPs to other parts of a protein, not just an end. With that modification, Lin anticipates that FLIPs could be created from most proteins that scientists want to investigate.

In science geeks, this is very interesting in that it converges two exciting fields: biological sensing, which has been dominated by fluorescent proteins, and optogenetics, the use of light to investigate biology,” Lin said.

In the past, scientists who specialized in biological sensing have tagged bits of the cellular machinery and then turned on at the flip of a light switch, but also tell an observer that they’re working. “One molecule can tell you what it is doing,” said Lin.

The trick to the new method is that it uses pieces of a Velcro-like fluorescent protein called Dropna.

In the dark, Dropna units adhere to each other and remain turned off. As the researchers begin to dim, Lin’s team spliced a Dropna unit to each of the proteins they wanted to study to make the FLIPs. In the dark, the Dropna units stuck together, but in light, the Dropna units released the proteins under study. When cyan-colored light was shone on the proteins, the Dropna units fell apart, exposing the proteins’ active sites so it could work.

“Using this method, you where it is and what it’s doing,” said Lin.

“The thinking in the field,” he said, “has been that the thalamus isn’t an integral part of the thalamocortical tract. It goes haywire during the recovery phase after a cortical stroke.” After all, he noted, in human studies, thalamocortical activity in the cerebral cortex are several inches apart. But the thalamus and the cortex are intimate partners in an ongoing two-way communication path, in which the thalamus receives signals from the outside world, tunes and bundles these signals into packets that it perpetually punts to relevant parts of the cortex, and then receives feedback from the cortex. Constant communication requires sturdy transmission lines, and the thalamus and cortex are connected via communication packets that transmit in opposite directions. The thalamocortical tract is the output line from the thalamus to the cortex.

The researchers’ first exploration in the stroke-affected rats, said research associate Jeanne Paz, PhD, the lead author of the new study, was the development of a contiguous device that could be permanently implanted in the thalamus, which occupies a much smaller terrain.

“We thought it might be superior to drug therapy, because it would not only respond instantly to seizures (while leaving the thalamus operate unimpeded during the intervening periods between seizures) but would target only a single group of cells immediately involved in the seizure circuitry, minimizing side effects. In addition, this new approach would not directly affect cerebral cortical function as all, thus further reducing side effects,” Huguenard cautioned, however, that any therapeutic applications in humans are still a decade off. “It would require inserting genes into people’s living brain cells. And we’re still a ways from being able to ensure the safety of gene therapy. This would also require being able to produce a reliable, battery-operated device that could be permanently implanted in the brain.”

However, Huguenard added, “Even a conventional device that very specifically targeted this small group of cells we’ve implicated would be a great step forward in epilepsy treatment.”

Additional co-authors are postdoctoral scholars Thomas Davidson PhD, and Eric Frechette, MD, PhD, research associate Isabel Parada, and former research assistant Kathy Peng. The study was funded by the NIH, and supported by the Molecular and Cellular Physiology and Neurological Sciences and of Molecular and Cellular Physiology.
Surgery helps child escape family history of heart problems

By Erin Digitalet

Tara Sharp will never forget the moment she received the sonogram results.

“The doctor said, ‘There’s something wrong with your baby’s heart. We don’t know if she will survive,’” Sharp said.

“I was devastated.”

Six months pregnant, Tara and her husband, Ben, were eagerly awaiting their second child. Now, instead of telling their older daughter to expect a sister, they were now preparing for the loss of a sibling.

A genetic counselor soon asked about family history of health problems. One aunt died in her late 20s from a heart condition, and a cousin died in her early 20s, with rare complex tetralogy of Fallot. The defect detected in a severe form on her sonogram was similar to her mother, Heather, revealed more: More than 50 babies on her family tree, including one of Heather’s own siblings, had died in infancy because of severe versions of the same heart defect. It was the first time Sharp had heard this extent of her family’s past.

But Sharp’s pediatric cardiologist in Santa Rosa, Calif., offered hope. “She told us that there were options.”

That cardiovascular surgeon, Frank Hanley, MD, who directs the hospital’s Children’s Heart Center, invented a surgical repair called unifocalization that has helped hundreds of children survive with complex tetralogy of Fallot. The defect affects several abnormalities in and around the pulmonary artery, including malaligned or malformed pulmonary artery to carry blood from the heart to the lungs. To correct it, the body develops “collateral” arteries that travel from the aorta to the lungs. This abnormal anatomy increases the pressure and risk of heart and lung damage. The defect also prevents the body from receiving fully oxygenated blood. Without surgical repair, most patients die in infancy or childhood.

Hanley’s approach was to deliver the baby, who would be named Elena, at Packard Children’s.

“Elena wouldn’t know the details of Elena’s collateral blood vessels until she was born and could receive cardiac catheterization,” said Hanley, who is a professor of pediatric cardiac surgery at the School of Medicine. “Most infants with this condition do not require urgent neonatal repair. But we know what needs to be done. So we wanted to assess Elena’s condition quickly.”

Hanley referred to the Center for Fetal and Maternal Health at Packard Children’s, where patient care coordinator Megan Hom Creamer works. After seeing her remaining prenatal care, including several diagnostic and consultative appointments with specialists, “we try to do everything we can to make the process less difficult,” Hom Creamer said, noting that some of Sharp’s monitoring was performed in Santa Rosa to spare her extra trips to Palo Alto. “We want the patient’s experience to be as simple, understandable and reassuring as possible.”

Sharp was scheduled to have a caesarean section shortly before her due date. But she went into labor three weeks early. After an emergency helicopter flight during labor, Sharp was glad to come through Packard Children’s doors and get settled into the room. “I felt relieved,” she said. “I thought, ‘We’re in the best hands possible; this is out of my control.’”

Elena’s birth by C-section went smoothly, but her early days were not easy. Almost immediately, she could breathe on her own, before the doctors could perform the catheterization to determine the severity of her congenital heart surgery, Sharp said. After 12 days in the neonatal intensive care unit, the new parent was able to con-
Reagan's treatment included medicines, hospitalization and chemotherapy. Nothing fixed the problem. Even the paper cut counts. She arrived at the emergency room. “We decided to do something definitive to help regain her quality of life,” said Glader, who is also a pediatric hematologist and oncology.

That meant removing Reagan's spleen, the site of platelet destruction. In 2010, minimally invasive surgery expert Sanjeev Dutta, MD, removed the organ through the girl's belly button in a no-scar procedure. “Since that time, she's been in remission and has definitively gotten her life back,” said Glader. Reagan's platelets are at normal levels and her activities are no longer restricted. The only drawback is that she lost the spleen's ability to fight some infections and so needs a little more medication for fevers, which can signal infections, Glader said. While Reagan's health was down, her singing was up: "She's got a beautiful voice," said Sandra. "Come Just As You Are" during Mass. "People said she brought tears to their eyes," said Sandra, who had no idea of her daughter's vocal power. The Sacred Heart Schools community started a prayer team for the girl who wasn't even allowed to ride a bike, and her illness inspired a blanket drive to assist children in need.

Word of Reagan's talent spread. She appeared on "Glee by the Bay" and the Herbst Theater's "That Kid Can Sing," and was the youngest of three winners in a 2012 competition of over 1,000 singers throughout California.

"That's really what I want to do," said Reagan excitedly. "I'd like to maybe be a singer who works with kids and then sings on the side."

"Our team has a lot of experience with cases like this," said Glader, who confirmed that he's planning to add Reagan to his iTunes playlist. "Helping to normalize a child's life is a guiding principle in everything we do, and we're happy to make this happen for such a talented young lady."

Reagan Claire Smith

Public invited to Dec. 6 open house for Hoover Pavilion

An open house at the newly renovated Hoover Pavilion, at 211 Quarry Road, is scheduled from 10 a.m. to noon on Dec. 6, and is free and open to the public, including medical center employees.

Amir Dan Rubin, president and CEO of Stanford Hospital & Clinics, will be among the speakers honoring the historic building's role in the community and at Stanford.

The event kicks off at 10 a.m. with a reception and refreshments. At 10:30 a.m., a ceremony will be held to mark the reopening of the building. From 11 a.m. to noon, there will be guided tours of the six-story, Art Deco building, which has been upgraded for modern medicine but whose distinctive architectural features have been preserved and restored. The building, which was constructed in 1930 as a research facility, served as the Shing center for Knowledge and Learning. It is free and open to the public, but limited. For more information, visit http://healthpolicyforum.stanford.edu or call 725-3359.

Gardner, PhD, an associate professor of medicine and director of nutrition studies at the Stanford Prevention Research Center, is involved in research focused on dietary interventions that attempt to test the effects of food components and food patterns on chronic disease risk factors, including body weight, blood lipids and inflammatory markers.

"Too often, the media and food companies lead us to believe that junk food is just a convenient meal, as opposed to a series of chemicals that can add up to a lifetime of health problems and obesity," Gardner said.

"We can only hope that people will get the message of our event and make the right choices for their future health."
Nolan wins funds to ‘map’ lineages in ovarian cancer cells

Garry Nolan, PhD, professor of microbiology and immunology, is the first recipient of the Ovarian Cancer Research Program’s Trail Innovator Award. The $1.2 million, five-year award, which is administered by the Department of Defense, is intended to advance the scientific understanding and treatment of ovarian cancer.

The OCRP is one of several Congressionally Directed Medical Research Programs. They represent a partnership among the DOD, Congress and the public to fund research into specific diseases or medical conditions. More than 90 research programs have been funded so far, focusing on topics as diverse as Alzheimer’s disease, Parkinson’s disease, schizophrenia, ovarian cancer, breast cancer and spinal cord injuries.

Nolan’s work focuses on the use of an innovative variation on a common cell-sorting technique called flow cytometry. He has devised a way — which he terms single-cell mass cytometry — to measure dozens of biological parameters, including cell size, DNA content and viability, in individual human cells. He plans to use it to identify family trees and lineage relationships among tumor cells in individual patients. The knowledge may one day be used to personalize ovarian cancer treatments.

“My laboratory and those of our collaborators are firmly committed to a large-scale effort in this malignancy,” Nolan said in an announcement by the OCRP. “Our message is that cancers cannot be orga- nized, can be mapped, and we finally understand which cells a given drug has activity against and map this to the molecular biology of the disease. We hope our work can overcome one or both of the major barriers (deeper classification and early detection) to improving therapeutic outcome for ovarian cancer patients.”

Flu continued from page 2

body recognizes the proteins as foreign and mounts an immune response that includes not only flu-specific antibodies, as there are two traditional vaccines, but also a cellular immune response.

“While the DNA approach may not get us all the way there, the combination of that technology plus a chance to in- vestigate how additional injection into the skin vs. muscle affects the response should provide valuable information to guide next steps in development of an improved influenza vaccine,” she said.

The NIH’s Vaccine Research Center first began studies of the DNA vaccine for influenza in 2006. Since then, more than 300 adults have received the center’s influenza DNA vaccines in eight different studies. More than 2,100 additional adults have received other types of the center’s DNA vaccines in 27 different studies for diseases such as HIV, Ebola, Marburg, SARS and West Nile.

The flu vaccine research study will be conducted in 330 participants at four research centers in the United States, with up to 100 of those at Stanford. Participants will be randomly assigned to receive any combination of DNA vaccine and/or seasonal flu vaccine (given either into the skin or into the muscle of the upper arm), and then be given a booster of the same type of licensed seasonal flu vaccine in the fall of 2013 with the new formulation. The study will last 68 weeks for participants not yet enrolled and include six clinic visits and two phone calls. The researchers will analyze participants’ blood samples to assess the amount of antibodies specific to the influenza viruses and will explore their T-cell responses to the influenza strains.

Participants must be healthy individu- als between the ages of 18 and 64 who have the ability to visit Stanford University Medical Center and have not yet received an influenza vaccine this flu season. Prospective participants can learn more online at http://vaccines.stanford.edu/clinical_trials/dnaVaccine. Information can also be requested by phone at 498-7284 and by email at Vaccines_Program@stanford.edu.

Participants will receive $30 for each non-vaccination clinic visit completed, and $60 for each vaccination visit completed.

OF NOTE

Porter

continued from page 1

the 200 staff members currently at the Stanford Menlo Park site will relocate just prior to the university’s winter break. This includes staff from the Human Resources Group, the Office of Finance and Administration, Information Resources & Technology, the Office of Facilities Planning and Management, the Office of Institutional Planning, the Research Management Group and the Office of Communication & Public Affairs.

They will be joined next summer by researchers in the departments of Radiology, Genetics and Pathology, as well as researchers from the stem medicine program.

Sam Gambhir, MD, PhD, professor and chair of radiology, said some 300 scientists in radiology, now housed at the Clark Center, the Lucas Center and Stanford Hospital will move to the new site.

The consolidation will help spur their work in early cancer detection, said Gambhir, who also directs the Canary Center at Stanford.

“The next generation of health care will be developed right here at Porter Drive,” he told a crowd at a recent town hall forum on the move.

The Department of Genetics will also move in its 13 state-of-the-art gene sequencing machines to the site, where researchers will labor to understand what humans are made of at the most basic level, said Michael Snyder, MD, professor and chair of genetics.

Both he and Gambhir invited the new Porter Drive staff to visit their laborato- ries, once they are up and running. Gambhir also said he hopes to get the new community involved in the annual Canary Center’s fund-raising bike ride and walk.

Randy Livingston, the university’s chief financial officer, also made a brief presentation at the town hall forum to explain the neighborhood made strategic and financial sense.

“Porter Drive will be our home for many years,” he said.

Stanford plans to redevelop the land (which is close to the Stanford Medicine Outpatient Center near U.S. 101) into new office space, though it is likely the build-out will not be completed for an- other seven to 10 years, and it remains unclear whether the university would oc- cupy the site or lease it to third parties, he said.

“Porter Drive will be our home for many years,” he said.

The buildings in blue represent the School of Medicine’s Technology & Innovation Park on Porter Drive, a few miles south of the main campus. The buildings in red are occupied by Stanford University offices.

The building in white represents the New Outpatient Center, which will be completed in 2014. The building in green represents the Stanford Neuroscience Building, which will be completed in 2015.

The building in orange represents the new Menlo Drive building, which will be completed in 2016. The building in purple represents the new Stanford Menlo Park site, which will be completed in 2017.

The building in yellow represents the new Stanford Hospital, which will be completed in 2018.

The building in red represents the new Menlo Drive building, which will be completed in 2019.

The building in green represents the new Stanford Hospital, which will be completed in 2020.

The building in purple represents the new Menlo Drive building, which will be completed in 2021.

The building in orange represents the new Menlo Drive building, which will be completed in 2022.

The building in yellow represents the new Menlo Drive building, which will be completed in 2023.

The building in blue represents the School of Medicine’s Technology & Innovation Park on Porter Drive, a few miles south of the main campus. The buildings in red are occupied by Stanford University offices.

The building in white represents the New Outpatient Center, which will be completed in 2014. The building in green represents the Stanford Neuroscience Building, which will be completed in 2015.

The building in orange represents the new Menlo Drive building, which will be completed in 2016. The building in purple represents the new Stanford Menlo Park site, which will be completed in 2017.

The building in red represents the new Stanford Menlo Park site, which will be completed in 2018.