More doctors tuned to ultrasound’s frequency

By Sara Wykes

In the public eye, ultrasound technology is probably best embodied by the big bedside machines that enable parents to catch a revelatory glimpse of their unborn babies.

Since the 1970s, however, ultrasound has become, quietly and steadily, the Swiss Army knife of health care, with an ever-expanding repertoire of functions, based on the ability of sound waves to travel through the body and bounce back when they hit something. Now the technology has been developed into a high-resolution, often pocket-sized aid for the diagnosis and treatment of many types of injuries and medical conditions.

Ultrasound’s trajectory has been mission creep of the best possible sort.

“You name the condition, and people are trying to diagnose or treat it with ultrasound,” said Pejman Gharahbaghian, MD, PhD, an assistant professor of radiology at the School of Medicine who employs MRI-guided, high-intensity-focused ultrasound to treat uterine fibroids. One of the main selling points of ultrasound for medical imaging and treatment is its lack of cancer-causing radiation.

Stanford has become a center of diagnostic ultrasound research, education and training. On Oct. 18, the school will host ULTrafest, a full day of free ultrasound instruction open to any medical student in the country. Experienced clinicians from several medical specialties will serve as teachers. Last year, more than 300 medical students from the western United States participated in the event.

The School of Medicine already has incorporated ultrasound into its anatomy training for first-year students and in its patient-doctor courses for pre-clinical students. The school will soon have a complete, four-year ultrasound curriculum, which will enable students to graduate with ultrasound competency.

The primary goal of ULTrafest, co-chaired by Lahle Gharahbaghian, MD, clinical associate professor of emergency medicine and director of Stanford Hospital’s emergency department ultrasound program, is to teach how ultrasound can enhance knowledge of anatomy, physiology and pathology — and, more importantly, how it can improve patient care in ways that Gharahbaghian has seen grow rapidly in the 14 years since she graduated from medical school.

“We use it for everything from head to toe and skin and organs,” she said. “It’s become an essential tool at the bedside we apply to immediately rule out—or rule in—medical conditions.”

Use in emergency medicine

Especially useful in emergency care, she said, is ultrasound’s ability “to help us find out what’s going on with a patient and to treat them appropriately with greater speed and accuracy.” She said, “We might have a patient, for instance, who is unconscious, incoherent or not speaking a language we know, and we have no idea why the heart rate is up and the blood pressure down.”

Seeing beyond the barrier of consciousness or language is another ultrasound capability, Gharahbaghian said. “Even if a patient’s eyes are swollen shut, you can use ultrasound to quickly see ultrasound,” page 6

Study: ‘Evolved’ protein may stop cancer from spreading

By Tom Abate

A team of Stanford researchers has developed a protein therapy that in mice was able to disrupt the process that causes cancer cells to break away from original tumor sites, travel through the bloodstream and start aggressive, new growths elsewhere in the body.

This process, known as metastasis, can cause cancer to spread with deadly effect.

“The majority of patients who succumb to cancer fall prey to metastatic forms of the disease,” said Jennifer Cochran, PhD, associate professor of bioengineering.

A paper describing the research was published online Sept. 21 in Nature Chemical Biology. Cochran and Amato Giaccia, PhD, professor of radiation oncology, share senior authorship of the paper. The lead author is Mihalis Karalis, a graduate student in Cochran’s lab.

Today, doctors try to slow or stop metastasis with chemotherapy.

See METASTASIS, page 7

Stem cells illuminate how mutation affects heart health

By Krista Conger

Over 500 million people worldwide carry a genetic mutation that disables a common metabolic protein called ALDH2. The mutation, which predominately occurs in people of East Asian descent, leads to an increased risk of heart disease and poorer outcomes after a heart attack. It also causes facial flushing when carriers drink alcohol.

Now researchers at the School of Medicine have learned for the first time specifically how the mutation affects heart health. They did so by comparing heart muscle cells made from induced pluripotent stem cells, or iPS cells, from people with the mutation versus those without the mutation. iPS cells are created in the laboratory from specialized adult cells, such as skin cells. They are “pluripotent,” meaning they can be coaxed to become any cell in the body.

“This study is one of the first to show that we can use iPS cells to study ethnic-specific differences among populations,” said Joseph Wu, MD, PhD, director of the Stanford Cardiovascular Institute and professor of medicine.

See MUTATION, page 7

Pregnant women have an unusually strong immune response to influenza, an unexpected finding from a new study.

Page 4

Published by the Office of Communication & Public Affairs
Stevenson named senior associate dean for maternal and child health

By Erin DIGITAL

David Stevenson, MD, the Harold K. Faber Professor of Pediatrics, has been appointed as the School of Medicine’s first senior associate dean for maternal and child health. He stepped into the role on Sept. 1.

“I’m excited to be launching an effort that allows me to focus on my interests in pediatrics and obstetrics,” Stevenson said. “We need increasingly strong integration between the vision and goals of the School of Medicine, on behalf of the school, and the vision and goals of Stanford Children’s Health. I’m looking forward to bringing my familiarity with Lucile Packard Children’s Hospital at Stanford, and its efforts to adapt to the changes it is facing, to the job of ensuring that those adaptations are coordinated with the school’s efforts around research and education.”

Stevenson, who also directs the hospital’s Fellowship Program for Pregnancy and Newborn Services, previously served for six years as the School of Medicine’s vice dean for academic affairs and has been a member of the faculty since 2012.

“David’s skill, expertise, compassion and dedication have made a real difference both in the lives of patients and to the reputation of Stanford Medicine,” said Lloyd Minor, MD, dean of the School of Medicine. “We are thrilled that he is bringing his talents to this new role.”

Stevenson’s portfolio will include all aspects of care for expectant mothers, fetuses and children. He will partner with Minor to lead the school’s collaborations with Stanford Children’s Health and the children’s hospital. In particular, he will be responsible for appointing associate or assistant deans, including a chief medical officer for the hospital to replace the current CMO, Kenneth Cox, MD, who plans to step down at the end of 2014.

Stevenson, a neonatologist, has been a member of the Stanford community for 35 years. His work in neonatal jaundice and the prevention of preterm birth has led to improved outcomes for countless infants and expectant mothers.

As an advocate for health, he has received a number of awards and honors and has been a member of the Institute of Medicine since 2012.

“I’m excited to be launching an effort that allows me to focus on my interests in pediatrics and obstetrics.” — David Stevenson, MD

Iris Gibbs appointed new associate dean for medical school admissions

By Tracie White

Iris Gibbs, MD, associate professor of radiation oncology, has been appointed associate dean for medical school admissions to replace Gabriel Garcia, MD, professor of gastroenterology and hepatology, who held the position for 15 years.

Her first day on the job was Sept. 2.

“I’m particularly excited about the opportunity to contribute to such an important aspect of shaping the future of Stanford Medicine.” — Iris Gibbs, MD

“I’m excited to be launching an effort that allows me to focus on my interests in pediatrics and obstetrics.” — David Stevenson, MD

From fashion magazine editor to dermatologist

A decade ago, Laurel Naversen Geraghty, MD, was writing feature articles for millions of readers, and enjoying the perks of working for glossy magazines — jetting to the Caribbean and Las Vegas, and attending celebrity-packed Manhattan fashion shows. As an editor at Glamour, life was fun and exciting. But after several years, she decided on a major career change.

GERAGHTY: I loved my work as a journalist. Writing articles about compelling news to help keep our readers informed was very fulfilling. Once, after I wrote an article about skin cancer for Glamour, the magazine received over 50 reader letters saying, “You helped me find my skin cancer!” That is incredibly rewarding. Skin care was one of my beats, and the more I covered dermatology and medicine, the more I found my self-missing science. And I decided to make a radical change to explore that interest.

When I said that I wanted to go to medical school, my colleagues looked at me like I had three heads. But I decided to explore that interest.

GERAGHTY: What do most people not know about dermatology?

GERAGHTY: When you think of people who use sunscreen, they naturally think of the common things — acne, eczema, warts, psoriasis. But dermatologists are trained to diag, pose and treat not only skin and hair, but also nails, and the backdrop to the exotic.

No matter what brings a patient into the office, skin cancer is always looking for skin cancer patients. It is the most common kind of cancer there is, and, if it is caught early, it is almost always curable.

Many patients worry that the medicated skin growth called a seborrheic keratosis. People really sweat it when they see it: ‘Are they going to get cancer?’

But any dermatologist can spot one in a second and know that it’s not a concerning mole or a cancer — it’s totally benign.

But there are things patients are not worried about that should be. Like how your spot’s changing or bleeding, or a sore that doesn’t heal, an ugly-ducking mole that looks different than its neighbors because of its shape, borders, color or size, get it checked out. It could be skin cancer.

Iris Gibbs: “I’m excited to be launching an effort that allows me to focus on my interests in pediatrics and obstetrics.” — David Stevenson, MD

So, acne, isn’t just for teenagers. We see tons of adults with acne in their 30s, 40s and 50s. There are many ways to treat acne, but the closest thing we have to a cure is called isotretinoin, commonly called Accutane. It’s an absolute life-changer and is a safe and predictable medication. Some patients are scared of it because of potential bowel problems or a reported risk depression, but the trials have demonstrated its safety. The exception is that patients should not get pregnant while taking the medication because it poses a high risk of birth defects.

Iris Gibbs: “I’m excited to be launching an effort that allows me to focus on my interests in pediatrics and obstetrics.” — David Stevenson, MD

GERAGHTY: Dermatologists believe that sunscreens are safe and that sunscreen is the single most important part of any person’s daily skin regimen. In California, just five minutes of sun exposure a day can raise your risk of skin cancer. I see that skin care can be prevention.

Dermatologists spend our professional lives diagnosing and treating skin cancer, so we become hypervigilant. I

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Rebuilding public trust is key to fighting Ebola virus in Africa

By Ruthann Richter

In the video, a man who has escaped an Ebola virus treatment center runs throughout the streets of Monrovia, Liberia, while an angry mob taunts the white physician who has come to calm the crowd and retrieve the patient. Workers dressed in green protective gear ultimately catch up with the patient, who is likely infectious, and force him into the back of a van, his legs flailing.

The dramatic video, filmed by CNN, demonstrates the widespread mistrust of the authorities in politically unstable areas of West Africa — one of the key factors that has led to the exponential spread of the Ebola virus there, Paul Wise, MD, MPH, a Stanford professor of pediatrics and a health policy expert, said during a panel discussion on the epidemic Sept. 23.

“Wise noted that in many of the affected areas, military and government officials have victimized communities for decades. Locals have protected themselves by avoiding involvement with the state.

“Control of Ebola will ultimately require political legitimacy, at least in the health sector. That’s what happened in Nigeria [where the epidemic appears contained], even with its corrupt government,” Wise told an overflow crowd gathered in the Walter J. Bremner Conference Center at Stanford. “You have to create treatment centers that are of the highest quality and that treat people with dignity — so people will want to go there, rather than escape.”

Grim forecast

Wise was among six panelists who addressed the myriad aspects of the epidemic, which Margaret Chan, MD, director general of the World Health Organization, has called “the greatest peace-time challenge” the organization has ever faced. The panel was sponsored by the Freeman Spogli Institute for International Studies and by Stanford Medicine.

Officially, more than 7,100 Ebola cases and 3,300 deaths from the disease have been reported in four countries: Liberia, Guinea, Sierra Leone and Nigeria. But panelists said those figures were likely underestimated. At the current rate of spread, in which the number of new infections is doubling every three to four weeks, the U.S. Centers for Disease Control and Prevention estimates that 1.4 million people could be infected by the end of January 2015 in the absence of dramatic interventions, said Douglas Owens, MD, a professor of medicine and director of the Center for Health Policy at FSU.

But even with “very aggressive” intervention, Owens said, it’s estimated there would be at least 25,000 cases by late December. If intervention is delayed by just one month, there will be 3,000 new cases every day; if it’s delayed by two months, there will be 10,000 new cases daily, he said. “It gives you a sense of the extraordinary urgency in terms of time,” Owens told the audience.

While the United States and other countries may feel as if they are doing their part, organizations are committing manpower and resources to fight the epidemic, the panelists emphasized the importance of building local health systems decimated by years of neglect. In Liberia, for instance, there are 92 doctors in a country of some 4 million people, said Michele Barry, MD, a professor of medicine and director of the Stanford Center for Innovation in Global Health.

The country’s only trained internist died of Ebola, as did the chief medical officer of the main hospital in Monrovia — both local leaders of the Yale/Stanford Johnson & Johnson Scholars program, in which physicians volunteer to respond to local health needs. “So it’s a tattered system,” she said.

Role of community workers

Tara Pertti, MD, a CDC epidemic intelligence service officer who worked this summer in both Guinea and Sierra Leone, said she spent time at a treatment center in Kenema, Sierra Leone, later returning to find that no one had been sent to help. “I received the terrible news that there were no physicians caring for approximately 90 patients at the treatment center,” she said.

She said mobilizing trusted community workers will be key to containing the epidemic. In Guinea, she traveled to a village north of the capital city of Conacry, where a young man who had recovered from the disease, which has a fatality rate as high as 70 percent. One of the men had lost five members of his family, but he had become a community advocate. He traveled with Pertti to a neighboring village, where they met a woman who was sick and whose son had died of the disease. “She was very fearful of going to the treatment center...but she was ultimately convinced to seek treatment. She recovered and was able to return home,” Pertti said.

The patient who survived was tremendously helpful because he could speak from experience and be credible. There needs to be more of these. In the forested region of Guinea, there are a lot of superstitions and different beliefs besides germ theory, and so it’s very challenging to go into those areas and help people understand that Ebola is a virus, it’s real, and we do have ways to help patients.

Even in the absence of sophisticated drugs, which are exceedingly scarce and untested in humans, simple methods of supportive care can be essential to survival, she noted. “Although there isn’t targeted therapy, IV fluids are very helpful,” Pertti said. “Many people die of shock, so it’s important to maintain blood pressure. Many have malaria, as well, and receive treatment. It’s important to get the message out that you have better odds of survival if you can get to a treatment center.”

Barry also advocated for the creation of a global health resource corps, a reserve group of physicians and nurses available to respond to major disease outbreaks like Ebola. While she lauded the enormous effort of private groups like Doctors Without Borders and Partners in Health, which have played a major role in battling the disease, their work has not been effectively coordinated on the ground.

“This has all been done in a disjointed, uncoordinated way,” Barry said. “It would be great to have a central global health strengthening fund, with a reserve of nurses and physicians who could sign up.”

Rebuilding public trust is key to fighting Ebola virus in Africa

Correction

In the Jan. 13 issue, a Q&A about clinical informatics failed to note that Sharon Geaghan, MD, associate professor emerita of pathology, was among the first physicians at Stanford or affiliated with Stanford to receive board certification in the subspecialty of clinical informatics. The oversight has been corrected in the online version of the Q&A, which was published Jan. 8.

Geraghty continued from page 2

there are two types of sunscreen: Chemical blockers absorb ultraviolet light, and physical blockers, such as zinc and titanium dioxide, reflect the sun’s light and are absorb ultraviolet light, and physical blockers, such as

Geraghty: When I went away to college, my mother told me she would not pay my tuition if I ever came home with a tattoo. So I never did.

Tattoos can be safe if done by a reputable professional using new and sterilized equipment. There is a risk of transmitting communicable diseases, including hepatitis, if needles are re-used or are not sterilized. There are a variety of different itchy, red, skin reactions that people can get from tattoo ink, especially red ink, which contains mercury sulfide, and that can be hard to get rid of when it is infected.

But tattoos don’t have to be forever. Skin lasers can break down tattoo ink within the skin, though the treatments can be painful and expensive. Some say the laser removal is more painful than getting the tattoo. Red tattoo ink is by far the most difficult color to remove and has had the highest rates of causing a skin reaction, though avoiding red may be a good choice.

5 What’s next for you? GERAGHTY: I am excited about the possibilities, and I am currently exploring options. I love practicing dermatology, getting to know my patients and helping Health workers check on a patient at an Ebola treatment unit in Liberia. Officially, more than 7,100 Ebola cases and 3,300 deaths from the disease have been reported in four countries.

Farmer: We should be saving the majority of Ebola patients

A slender, weakened Ebola patient sits alone, head in his hands, on the floor of a darkened room in an abandoned treatment center in West Africa. That is the unfortunate portrait of Ebola care in the region today — an emaciated system completely incapable of containing the rapidly spreading virus, renowned physician and humanitarian Paul Farmer told a Stanford audience Oct. 3, referring to a photo projected on a screen behind him.

Almost no [care] delivery has occurred around Ebola,” said Farmer, MD, PhD, who recently returned from Liberia, where his Partners in Health organization is working to combat the epidemic. “There is not a lot of T [treatment] and not a lot of C [care] in Ebola care units. If you don’t have the resources, you’re not going to have the stuff, the space, the staff you need. I think the least we could do is have a safety net for everybody... We should be saving the majority of patients,” he told an audience of some 400 people in an auditorium at the Stanford Graduate School of Business.

He said the West Africa epidemic is unfortunately symptomatic of stark global inequities in health care. “That’s the issue he and his group have so ably addressed in Haiti and Rwanda.”

In Haiti, for example, after the only nursing school was reduced to rubble in the 2010 earthquake, his team built a medical center and teaching hospital — an expansive, modern complex in a rural area of the country, he said to applause from the audience.

“‘This is what I think of for rural Liberia, rural Sierra Leone,” said Farmer, who is also a professor of global health and social medicine at Harvard. “This is not rocket science. Just think what we could do if we had a lot of help with systems and partners. It just requires sticking with some of these problems for a long time.”

Are tattoos safe? They’re everywhere. And do you know what your patients are getting?

4 Are tattoos safe? They’re everywhere. And do you know what your patients are getting?
Immune response turned up high by flu during pregnancy

By Erin Digitale

Pregnant women have an unusually strong immune response to influenza, an unexpected finding that may explain why they get sicker from the flu than other healthy adults, new research from the School of Medicine and Lucile Packard Children's Hospital Stanford has found.

The results were surprising because immune responses are thought to be weakened by pregnancy to prevent the woman's body from rejecting her fetus.

The study, published online Sept. 22 in the Proceedings of the National Academy of Sciences, is the first to examine the reactions of immune cells taken from pregnant women to influenza viruses, including the H1N1 strain that caused the 2009 flu pandemic.

“We were surprised by the overall finding,” said Catherine Bliss, MD, PhD, assistant professor of infectious diseases and the study's senior author. “We now understand that influenza in pregnancy is a hyperinflammatory disease rather than a state of immunodeficiency. This means that treatment of flu in pregnancy might have more to do with modulating the immune response than worrying about viral replication.”

In the study, immune cells taken from 21 pregnant women and 29 healthy, nonpregnant women were exposed to different flu viruses in the lab. The immune cells were obtained by collecting blood samples from the women before and seven days after they received flu vaccines. Cells taken from pregnant women six weeks after their babies were delivered were also tested. The researchers studied responses to two flu viruses: pandemic H1N1 and a strain of seasonal influenza, H3N2.

Bad effects on lungs

Pregnancy enhanced the immune response to H1N1 of two types of white blood cells: natural killer and T cells. Compared with the same cells from nonpregnant women, H1N1 caused pregnant women's NK and T cells to produce more cytokines and chemokines, molecules that help attract other immune cells to the site of an infection.

“If the chemokine levels are too high, that can bring in too many immune cells,” Bliss said. “That’s a bad thing in a lung where you need air space.”

Getting the flu during pregnancy, especially pandemic strains such as those that caused the pandemics of 1918, 1957 and 2009, can carry a heightened risk for pneumonia and death, she noted.

Both strains of flu also caused NK and T cells to be activated in a greater variety of ways in pregnant than nonpregnant women, the study found.

Today, pregnant women with influenza are usually treated with drugs to slow the replication of the flu virus in their bodies. Although this is a useful treatment, the new findings suggest that it isn’t the only good option, the study’s authors said.

“If our finding ends up bearing out in future studies, it opens the possibility that we can develop new immune-modulating treatment approaches in the setting of severe influenza, especially in pregnant women,” said Alexander Kay, MD, instructor in pediatrics.

Increased outreach

In recent years, the biosciences office of graduate education has broadly increased its outreach efforts to underrepresented students, including low-income students, students who would be the first in their families to attend graduate school, students with disabilities and students who self-identify as LGBTQ.

The office also has encouraged greater outreach from faculty and has added elements of graduate school application preparation — such as an increased focus on GRE test-taking skills and mock interview practice — to a nine-week, research-intensive residential program for undergraduates interested in graduate degrees in the biosciences.

Known as the Stanford Summer Research Program/Amen Scholar Program, it serves as a pipeline to Stanford and other top graduate programs across the country.

Efforts also included the formation of the Biosciences Diversity Advisory Council, made up of faculty and admissions chairs, whose mission is to develop...
Family-based therapies can treat anorexia in teens, study finds

By Erin DIGITAL

Two different family-based therapies are both effective at combating anorexia nervosa in teenagers, according to the largest study ever to compare two such treatments for the life-threatening eating disorder.

The findings, from a multisite study led by researchers at the School of Medicine, add to a growing body of evidence supporting the value of parents’ involvement in anorexia treatment.

The results, published Sept. 24 in JAMA Psychiatry, follow prior Stanford research that found a family-based approach was twice as effective as individual therapy for treating adolescent anorexia patients.

“arise the message for parents is that, first, there is good treatment available for their child who is struggling with anorexia,” said Stewart Agras, MD, professor emeritus of psychiatry and behavioral sciences at Stanford and the lead author of the new study. “Second, the preferred treatment is family-based therapy in which parents help their child regain weight.”

Involving, not blaming, families

Anorexia nervosa patients suffer from distorted body image, erroneously believing they are overweight. They overexercise and refuse to eat enough to maintain a healthy body weight. The disease, which affects about 0.5 to 0.7 percent of adolescent girls, has one of the highest suicide rates of any psychiatric disorder.

For a long time, people blamed families for causing anorexia and thought they should be left out of treatment,” said James Lock, MD, PhD, professor of psychiatry and behavioral sciences at Stanford and a co-author of the study. “But this study suggests that, however you approach it, involving the patient’s family can be useful, and that more focused family treatment works faster and more cost-effectively for most patients.”

Lock also receives royalties from Guildford Press for a comprehensive Eating Disorders Program at Lucile Packard Children’s Hospital Stanford.

The study, a randomized, controlled trial of 164 patients conducted at six sites in the United States and Canada, compared two forms of anorexia treatment that involved regular therapy sessions with adolescents and their families.

One approach focused on teaching parents to help their children eat normally and regain weight at home. The other therapy attempted to resolve difficult family dynamics. Both therapies produced similar rates of recovery from anorexia.

The patients were ages 12-18 and had been ill with anorexia for an average of 13.5 months. At the start of the study, all patients had body weights of at least 75 percent of what was considered ideal, meaning that physicians considered it safe for them to receive outpatient treatment. Nearly 90 percent of the patients were female. All had at least one parent who agreed to participate in treatment. The nine-month trial consisted of 16 one-hour therapy sessions over a nine-month period. The success of the treatments was evaluated at the end of the nine-month period and one year later.

In both forms of family therapy, patients experienced similar weight gain by the end of treatment and at the one-year follow-up. The therapy that focused on teaching parents to help their children eat normally again was about half as expensive as the family-dynamics approach, mostly because patients spent less time in the hospital. However, the therapy that focused on family dynamics was more effective for one specific subgroup of patients: those who also had severe symptoms of obsessive-compulsive disorder.

Hope for long-term remission

Lock, who has conducted several prior studies of the therapy that teaches parents to help their children eat normally again, said he thinks this approach works by interrupting the patient’s behaviors that are supporting erroneous thinking patterns. “We think that parents are able to disrupt the maintaining behaviors of anorexia long enough that the thoughts and cognitions that go with the disease diminish,” he said. “At that point, the cognitions themselves have very little staying power.”

Addressing anorexia during the teenage years offers the best hope for long-term remission, Agras said.

“The longer anorexia goes on, the more difficult it is to treat,” he said. “A great many people live chronically restricted lives because of this disease — they plan their days around undereating and overexercise — and quite a few die. The idea is to treat the disorder in adolescence to prevent more adults from becoming anorexic.”

Other Stanford co-authors of the study are statisticians Bryan Syron, MS, and Boool Jo, PhD, associate professor of psychiatry and behavioral sciences. Lock is a member of the Child Health Research Institute at Stanford.

The study was funded by the National Institute of Mental Health. Agras and Lock receive royalties from Oxford University Press for contributions to a textbook about eating disorders.

Lock also receives royalties from Guilford Press for books he has written about family-based treatment for anorexia nervosa and bulimia nervosa, and payments from the Training Institute for Child and Adolescent Eating Disorders, where he is a faculty member who trains other clinicians in evidence-based treatment methods for eating disorders.

Stanford’s Department of Psychiatry and Behavioral Sciences also supported the work. Inside Stanford Medicine October 6, 2014
Ultrasound
continued from page 1

ultrasound has proven more accurate than a chest X-ray
mocne to its imaging prowess: the lungs. In the air-filled
narrowing plaque than is coronary angiography, and for
prostate cancer biopsies and emergency procedures
bation, fine needle aspiration, interventional radiology
several nursing units. The Life Flight helicopter also
at the Stanford Cancer Center, the Cath-Angio Lab and
sound devices. Ultrasound is also standard equipment
anesthesia, urology, outpatient surgery, mammography,
ology and infertility, respiratory therapy, orthopaedics,
and postoperative care in the ICU. Ultrasound is also
diovascular issues.

The long list of other invasive procedures made less
complicated by ultrasound includes endotracheal intuba-
tion, needle aspiration, interventional radiology
procedures, pedicle screw insertion in scoliosis surgery,
prostate cancer biopsies and emergency procedures
like central venous access. Ultrasound also is a much
gerder and quicker screening tool for sports artery-
arrowing plaque that is coronary angiography is common
.resume at atarial issues before neck surgery.

Some ultrasound is also relatively inexpensive: Even a re-
 refurbished CT scanner with a minimum view capacity is
leased at $65,000. New ones start at $90,000. Hand-
old ultrasound can cost as little as $7,000; laptop-
device used range from $25,000 to $40,000.

More recently, the use of ultrasound has crossed into
angiography, enabling doctors to image the anatomy of a
mune to its imaging prowess: the lungs. In the air-filled
environment of the lungs, the sounds wave that are
are the hallmark of this field. Ultrasound can ping a few
However, in lungs where disease has produced fluids, ultrasound
proven more accurate than a chest X-ray and
scan to diagnose common lung con-
, including pulmonary edema, pneumonia and pleural effusions.

Ultrasound devices at Stanford are so highly detailed
that “it’s not easy to keep spaces,” said Harvey Fortune,
assistant director of Stanford Health Care’s clinical
technology group.

Gharahbaghian and other Stanford physician-scientists
are pushing medical ultrasound to the next level. He
and his colleagues, Jamie Henderson, MD, professor of
urology, and Casey Halpern, MD, assistant pro-
 of neurosurgery, are using high-intensity-focused ultrasound,
guided by MRI, to treat essential tremor,
a nervous system disorder marked by uncontrollable
shaking. The ultrasound heats and destroys specific
brain tissue: No anesthesia, no scalp incisions, no burr
holes through the skull. Another team of Stanford phy-
sicians, which includes radiologists, neurosurgeons,
ocologists and physicists, plans to conduct an
investigatory test of this technology, available only at
a handful of medical centers worldwide, to allow drugs
to cross the blood-brain barrier for more targeted treat-
ment of brain tumors.

Ultrasound is an essential part of the work of Adam
de la Zerda, PhD, an assistant professor of structural bi-
ology. In collaboration with Sam Gambhir, MD, PhD,
professor and chair of radiology, de la Zerda recently de-
veloped and patented a technology called phonoacous-
tic imaging that transforms light waves into ultrasound
waves. Its goal is to detect cancer with a resolution that
matches CT scanning and MRI.

Quick answers for patients

Viveta Lobö, MD, who completed a fellowship in
ultrasound in Stanford’s emergency department and
serves as an ULTRAfest co-chair, said studies have
shown patients feel that doctors using bedside ultra-
sound spend more time at patients’ bedside.

Studies also have shown that hospitalized patients who
underwent ultrasound scanning were discharged
more quickly.

Ultrasound can also provide quick answers, which
patients appreciate. “I can tell someone right away that
there are no gallstones, or that a woman’s baby is OK,”
Lobo said. Even more crucial, she said, “we can see and
treat quickly that life-threatening ectopic pregnancy or
large pulmonary embolism.

But ultrasound takes some training to master, Lobö
added. “You have to know how to get good images —
how to move it around obstacles, like the ribs, to see
what you need to see. You have to know how to adjust
the settings, just as you do in photography. Then you
have to know how to interpret what you’ve seen.”

Gharahbaghian is seeing more and more community
physicians, as well as those in outpatient clinics, who
are using ultrasound. She hopes that trend continues.
“The more we spread the news of how ultrasound helps
patients in all clinical settings, the better,” she said.

Sara Wykes is a writer in the communications office at
Stanford Health Care.

End-of-life decision-making will be the topic of con-
versation between two physicians — one an expert in
palliative care, the other a neurosurgeon who has been
diagnosed with lung cancer — at the 24th annual Jona-
than J. King Lecture at 5:30 p.m. Oct. 21 in Berg Hall
at the Li Ka Shing Center.

The event, titled “Discussing Palliative Care Earlier:
A Conversation Between Dr. Kalanithi and Dr. Quill,”
is free and open to the public.

Timothy Quill, MD, an expert on the doctor-patient
relationship and palliative care, is a professor medicine,
of psychiatry and of medical humanities at the Univer-
sity of Rochester School of Medicine and Dentistry. He
will talk with Paul Kalanithi, MD, who was recently
a postdoctoral scholar and neurosurgery resident at
Stanford.

Quill has published and lectured widely about end-
of-life care topics, including delivering bad news, dis-
cussing palliative care earlier, and exploring lost-regret
options. He is the author of several books about end-
of-life matters.

Kalanithi wrote an opinion piece, published Jan 24.
Left?” in which he discussed what it was like viewing his
own CT scan as both a doctor who delivers bad news to
patients and as a patient diagnosed with cancer.

For more information, go to http://bioethics.stan-
ford.edu or call 723-5760.

Palliative care subject of King Lecture Oct. 21
Metastasis
continued from page 1

terms of cardiovascular medicine and of radiology.

Some findings may help us discover new therapeutic paths for heart disease for carriers of this mutation," said Wu. "In the future, I believe we will have banks of iPS cells generated from many different ethnic groups. Drug compa-
nies or academic institutions that recruit members of different ethnic groups re-
spond to drugs or study, how one group might differ from another, or design specific drugs to fit particular groups.

The findings are described in a paper published Sept. 24 in the Journal of the American College of Cardiology and are supported by the NIH, the American Heart Association and the Foundation for Heart Disease Research.

Wu and Diana Mochly-
Rosen, PhD, professor of chemical and systems biology, co-authored the paper, and postdoctoral scholar An-

tje Ebert, PhD, is the lead author.

ALDH2 and cell death

The study showed that the ALDH2 mutation affects heart health by con-
trolling the survival decision cells make during times of stress. It is the first time ALDH2, which is involved in many common metabolic processes in cells of all types, has been shown to play a role in cell survival. In particular, ALDH2 activity, or the lack of it, influ-
ences whether a cell enters a state of pro-
grammed cell death called apoptosis in re-
sponse to stressful growing conditions.

In this study, Ebert and her colleagues first studied the skin cells obtained from five East Asian males and females with an ALDH2 and five East Asian males and females with a normal copy of the gene, they are

People have studied the enzyme ALDH2 for many years in animal mod-
el, said Ebert. "But there are many differences in how the enzyme behaves in humans. Now we can study actual human heart muscle cells, conveniently grown in the lab."

The iPS cells in this study were cre-
ated from skin samples donated by 10 men, ages 21-22, of East Asian descent. About 8 percent of the world's popu-
lation carries the mutation in one or the other copy of the ALDH2 gene, which encodes a protein known as aldehyde dehydrogenase 2. The enzyme can remove short-circuits the production of the functional protein. The ALDH2 gene has this one normal and one mutated copy of the gene, they are

"The decoy attaches to Gas6 up to a
tighten its grip on Gas6, rendering the decoy interaction virtually irreversible. Kariolis made other tweaks to en-

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Immune activity shortly after surgery big clue to recovery rate

By Bruce Goldman

The millions of people who undergo major surgery each year have no way of knowing how long it will take them to recover from the operation. Some will feel better within days. For others, it will take a month or more. Right now, doctors can’t tell individual patients which category they will fit into.

Now, researchers at the School of Medicine have discovered that the activity level of a small set of immune cells during the first 24 hours after surgery provides strong clues on how quickly patients will bounce back from surgery-induced fatigue and pain, and be back on their feet again.

The finding, based on an in-depth analysis of blood samples drawn from middle-aged to older patients un- dergoing a hip-replacement procedure, is described in a study published Sept. 24 in Science Translational Medicine. The study may be the most comprehensive character- ization to date of the immune system’s response to trauma.

The Stanford researchers were able to make this discovery because they used a highly sensitive technol- ogy called single-cell mass cytometry. Developed in the laboratory of microbiology and immunology professor Garry Nolan, PhD, the method enables simultaneous monitoring of large numbers of biochemical features both on the surfaces of immune cells and within the cells, telling the scientists not only what kind of cells they are looking at but how active they are.

Strong clues in first 24 hours

“We learned that within the first 24 hours after sur- gery you can find strong clues in blood that reveal what shape a particular patient is going to be in two weeks later,” said Martin Angst, MD, professor of anesthesiol- ogy, pain and perioperative medicine, who shared se- nior authorship of the study with Nolan.

The discovery could lead to the development of a personalized diagnostic blood test for predicting recov- ery after major surgery. (Stanford owns a provisional patent on the associated intellectual property.) Such a diagnostic could both help physicians make early deci- sions about which patients to put on enhanced recov- ery programs and help recovering veterans know what to tell loved ones and bosses to expect. A full understanding of the molecular mechanisms identi- fied in the study might even make it possible for cli- nicians to manipulate the immune system so as to foster faster recoveries.

Most of the more than 200 million surgical procedures performed annually worldwide are minor, Angst said. But in the United States alone, millions of those procedures — hip replacements, for example — are suf- ficiently traumatic to trigger profound inflammatory responses in patients.

Healing versus impeding

That initial blast of inflammation is essential to the healing process, said Angst. “You need to unleash the dragon,” he said. “But you need to be able to ride in too much inflamm- ation spells a pre- tracted recovery.”

The immune system’s components must continually rebalance their contributions in a dynamic fashion, rather than impedes healing.

A few years ago, a new trend emerged in the study with Nolan explaining mass cytometry, which permits simul- taneous measure- ments of more than 50 different surface and internal features of single cells, while standard cell-sorting methods typically max out at 12-15 such measurements. This triggered a collabora- tion between Angst and Nolan, whose specialties were bridged by postdoctoral scholar Brice Gaudilliere, MD, PhD, now a clinical instructor in anesthesiology. Gaudilliere shared lead authorship of the study with Gabriela Fra- guadakis, a graduate student in Nolan’s lab.

This ability to comb through so many features at once gives researchers a window to a cell’s soul, said Nolan, who is the Rachford and Carlota Harris Professor. “We can ob- serve not only an immune cell’s identity but its state of mind,” he said. Nolan holds an equity posi- tion in Fluidigm, a company that makes technology to measure single-cell cytometry in- strumentation and reagents used in the study.

The study recruited 32 otherwise healthy patients, mostly between ages 50 and 80, who were undergoing first-time hip-replacement procedures carried out by Stanford orthopaedic surgeons. Blood samples from these patients were drawn one hour before surgery, then at one, 24 and 72 hours post-surgery and again four to six weeks after surgery. These samples were quickly de- livered to Nolan’s lab, where cytometric analysis of 35 features in and on each sample’s roughly half-million constituent cells yielded profiles of the cells’ identities along with key activities underway inside them.

Every three days for a full six weeks after surgery, patients filled out questionnaires probing the degree of pain and fatigue they were experiencing and how well their refurbished hip was functioning.

Zeroin on in key predictor

The Stanford team observed what Angst called “a very well-orchestrated, cell-type- and time-specific pattern of immune response to surgery.” The pattern and a sequence of events detected rises and falls in numbers of diverse immune-cell types, along with vari- ous changes in activity within each cell type.

“Amazingly, this post-surgical signature showed up in sleep apnea patients after surgical intervention.”

MAURICE OHAYON, MD, DSc, PhD, was appointed professor of psychiatry and behavioral sciences, with tenure, effective Aug. 1. The focus of his research is the epidemiology of sleep and psy- chiatric disorders. He serves as chief of the Division of Public Mental Health and Population Sciences and director of the Stanford Sleep Epidemiology Research Center. He is the Rachford and Carlota Harris Professor.

LUCY SHAPIRO, PhD, the Virginia and D. K. Ludwig Profes- sor and director of the Beckman Center for Molecular and Genetic Medicine, will receive the 2014 Pearl Mei- ster Greengard Prize. The annual award, which celebrates the achievements of outstanding women in science, will be presented on Nov. 11 at Rockefeller University in New York City. Shapiro is be- ing honored for her pioneer- ing work on the single-celled Caulobacter bacterium, which illustrates how cell-surface mechanisms that control the differentiation of cells in all living things, from the simplest organisms to the most complex, use.

The Stanford group is now looking to see if they can identify a pre-operation immune signature that predicts the rate of recovery. “If we could predict recovery time before surgery even took place,” said Gaudilliere, “we might be able to see who benefit from boosting their immune strength beforehand, or from pre-surgery in- terventions such as physical therapy. It might even help us decide when or if a patient should have surgery.”

The study was supported by Stanford’s Department of Anesthesiology, Pain and Perioperative Medicine; the California Institute for Regenerative Medicine; the European Commission; the U.S. Food and Drug Agency; the Department of Defense; and the National Institutes of Health.

Other Stanford co-authors of the study are orthopaedic surgery professor Stuart Goodman, MD, PhD; orthopaedic surgery associate professor James Huddleston, MD; microbiology and immunol- ogy professor Mark Davis, PhD; assistant professor of pathology Sean Bendall, PhD; obstetrics and gynecol- ogy assistant professor Wendy Fantl, PhD; research associate Monica Nicolas, PhD; and Edward Czarny, PhD; data analyst Rachel Finck; postdoctoral scholar Robert Brugnert, PhD; research nurse Martha Tingle; social-science research assistant Julian Silva; and biol- ogy undergraduate Christine Yeh.