In treating crash victims, readiness paid off

By Rosanne Spector and Robert Dicks

“Did you know there’s been a plane crash at San Francisco airport?”

It was a little past 11:30 a.m. on July 6 when Eric A. Weiss, MD, the medical director of the joint office of emergency management for Stanford Hospital & Clinics and Lucille Packard Children’s Hospital, first learned of the crash landing of Asiana Flight 214. A television in the emergency department waiting room had reported the news, which made its way to the director of pediatric emergency medicine, Bernard Dannenberg, MD, and then to Weiss, both of whom, fortuitously, were working in the ED that day.

Weiss knew that if there were casualties, Stanford — one of only two level-1 trauma centers within 25 miles of the airport, and the only one with a helicopter-landing pad — would be well-equipped to treat them.

An attending physician in the Marc and Laura Andreessen Emergency Department at Stanford, Weiss had a committed, well-drilled staff to work with, and many key emergency responders were already on site or immediately available.

At 11:50 a.m., the emergency department got a call from San Mateo County Emergency Ser-

Medical responders and support staff wait in front of Stanford’s emergency department for victims of the July 6 crash of Asiana Flight 214 to begin arriving.

Company payments to doctors to be made public next year

Information on amounts over $10 will be compiled starting Aug. 1

By Ruthann Richter

Beginning Aug. 1, pharmaceutical and medical-device companies will collect information about their payments to doctors and teaching hospitals for publication in a public online database, which is scheduled to go live next year.

The Physician Patients Sunshine Act, passed in March 2010 as part of the Affordable Care Act, requires these companies to disclose to the federal government and the public payments over $10 to physicians and teaching hospitals every year. This includes consulting fees; honoraria; gifts; compensation for food, travel, education or conferences; research funding; stock or stock options; investment income; royalties; and licenses.

The law is intended to create more transparency in industry-provider relations. It aims to help consumers make better informed decisions and alert them to physicians’ potential conflicts of interest, which can be detrimental to care and contribute to higher health-care costs. But given the very large volume and complexity of data involved, there is concern among both industry and physician groups about the potential for errors in the new system, which could lead to confusion among consumers.

“Faculty should be aware that virtually all payments made to physicians from companies are going to become a matter of public knowledge and availability,” said Harry Greenberg, MD, senior associate dean for research at the School of Medicine. “I am hopeful that the specific purpose for the payments will be clear and accurate in the public database. For instance, the law requires companies to report payments for specific research projects, which would be totally appropriate and important. Such payments, of course, are made to Stanford University, not the individual PI. The university then uses them to fund specific research projects. It also includes reporting of payments for participation in speakers’ bureaus, which is something not

Mammals can ‘choose’ sex of offspring, researchers find

By Ruthann Richter

A new study led by a researcher at the School of Medicine shows that mammalian species can “choose” the sex of their offspring in order to bear the odds and produce extra grandchildren.

In analyzing 90 years of breeding records from the San Diego Zoo, the researchers were able to prove for the first time what has been a fundamental theory of evolutionary biology: that mammals rely on some unknown physiologic mechanism to manipulate the sex ratios of their offspring as part of a highly adaptive evolutionary strategy.

“This is one of the holy grails of modern evolutionary biology — finding the data which definitively show that when females choose the sex of their offspring, they are doing so strategically to produce more grandchildren,” said Joseph Garner, PhD, associate professor of comparative medicine and senior author of the study, published July 10 in PLOS ONE. The results applied across 198 different species.

The scientists assembled three-generation pedigrees of more than 2,300 animals and found that grandmothers and grandfathers were able to strategically choose to give birth to sons, if those sons would be high-quality and in turn reward them

Study hints at possible diabetes vaccine

By Bruce Goldman

A clinical trial of a vaccine, led by researchers at the School of Medicine and designed to combat type-1 diabetes, has delivered initially promising results, suggesting that it may selectively counter the errant immune response that causes the disease.

Several important findings of the multicenter, randomized, double-blind trial were published June 26 in Science Translational Medicine. First, levels of a blood-borne proxy of insulin production were maintained — and in some cases increased — over the course of the 12-week dosing regimen. This indicates that those getting the vaccine may have suffered less ongoing destruction of beta cells, which produce and secrete the hormone insulin after a meal, than those given placebo injections. (A peptide is a very short protein sequence.)

Second, blood levels of a specific group of immune cells that inappropriate ly home in on and destroy a protein found only on beta cells appear to have been selectively depleted in patients receiving

See CRASH, page 4

See SUNSHINE, page 7

See CRASH, page 4

See VACCINE, page 8
A new, noninvasive technique for tracking stem cells after transplantation — developed by a cross-disciplinary team of radiologists, statisticians and materials scientists at the School of Medicine — could help surgeons determine whether a procedure to repair injured or worn-knee is successful.

The technique, described in a study published online on July 15, relies on an imaging agent already approved by the U.S. Food and Drug Administration for an entirely different purpose: anemia treatment. Although this study used rodents, the approach is likely to be adapted for use in humans this fall as part of a clinical trial in which mesenchymal stem cells will be delivered to the site of patients’ knee injuries. Mesenchymal stem cells are capable of differentiating into bone and cartilage, as well as muscle, fat and tendon, but not into other cell types that populate the knee.

Every year, arthritics account for 4 million outpatient visits and 700,000 knee-replacement procedures. But the early repair of cartilage defects in young patients may prevent further deterioration of the joint and the need for knee replacement later in life, said the study’s senior author, Heike Daldrup-Link, MD, PhD, an associate professor of radiology and clinician who splits her time between orthopaedic surgery and research and treating patients.

“Satellite cells can sit around for practically the entire life span of any tissue, doing nothing of anything. But they’re ready to transform to an activated state as soon as they get word that the tissue needs repair,” Rando said. “It seemed to us that the signals that tell satellite cells to become activated could be used to provide a noninvasive way to track the youngness of stem cells.”

The researchers harvested satellite cells from both healthy and injured muscle tissue of young mice and from healthy tissue of old mice; extracted these cells’ DNA with the histone coatings intact; and used tagged antibodies targeting the different kinds of marks to find which spots on those histones were flagged with either “stop” or “go” signals.

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Instead, they found, in quiescent satellite cells taken from the younger mice, copious instances in which histone in the vicinity of genes already closely regulated by other tissues were marked with both “stop” and “go” signals, just as genes associated with development to mature-muscle status were. One reason why we’re not looking for that, and we certainly weren’t expecting it,” Rando said. “We figured all the muscle genes would be either poised for activity — marked with both ‘on’ and ‘off’ signals — or ‘on’, and that all the other genes would be turned off. But when you look at these satellite cells the way we did, they seem ready to become all kinds of cells. It’s a mystery,” he said, suggesting that it could mean stem cells thought to be committed to a particular lineage may be capable of becoming other types of tissue entirely.

“We haven’t the answers yet. But now that we know what kinds of changes occur as these cells age, we could ask which of these changes are important in aging. We could then say, ‘What can we do about it?’”

The differences between quiescent satellite cells and Rando’s team found, are mirrored by those between young and old quiescent satellite cells. “With there’s an uptick in repressive markers. A lot more genes are locked in the off position,” he said.

The meaning of this is not yet clear, he added. “In a division-capable cell, as opposed to the nondividing, differentiated muscle cells that activated satellite cells may someday become, it may be important to maintain a high level of repression with age. Maybe this increase in repression is a kind of retro-silencing mechanism, keeping aging satellite cells — which could have accumulated some dangerous mutations over the years — in a state of dormancy. But more work needs to be done before we can say anything meaningful,” Rando said.

The description of the histone-code differences between young and old cells constitutes a yardstick allowing investigators to ask which of these differences are important in aging. “We’re interested in figuring out how an old cell goes back to becoming a young cell” — as appeared to be the case when tissues of older mice were exposed to blood from young mice, Rando said. “Rando’s group is now looking to test whether the signatures they’ve identified in satellite cells generalize to other kinds of adult stem cells as well. The Glenc Foundation and the National Institutes of Health funded the study, whose lead author was postdoctoral scholar Lini Liu, PhD. The other co-authors, all non Stanford, are an associate professor of genetics Anne Brunner, PhD; postdoctoral scholar Tom Cheung, PhD; MD/PhD student Gregory Charville; and research assistants Bernadette Marie Ceniza Hurgo, Tripp Leavitt and Johnathan Shih.

The Department of Neurology and Neurological Sciences also supported the work.

The technical novelty to curiosity about exactly what is happening inside a cell to rejuvenate it, said Rando. One likely place to do that was histones, he thought, but this is where the meaning of this is not yet clear, he added. “In a division-capable cell, as opposed to the nondividing, differentiated muscle cells that activated satellite cells may someday become, it may be important to maintain a high level of repression with age. Maybe this increase in repression is a kind of retro-silencing mechanism, keeping aging satellite cells — which could have accumulated some dangerous mutations over the years — in a state of dormancy. But more work needs to be done before we can say anything meaningful,” Rando said.

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Long-term hearing loss from loud explosions, such as blasts from roadside bombs, can be irreversible as previously thought, according to a new study by researchers at the School of Medicine.

Using a mouse model, the study found that loud blasts actually cause hair-cell and nerve-cell damage, rather than structural damage, to the cochlea, which is the auditory portion of the inner ear. This could be good news for the military, which has found that soldiers who, after surviving these often devastating bombs, suffer long-term hearing damage.

“This is surprising because we thought we should try to reduce this damage,” said John Oghalai, MD, associate professor of otolaryngology and senior author of the study, which was published July 1 in PLOS ONE. “If the cochlea, an extremely delicate structure, had been shredded and ripped apart by a large blast, as earlier studies have asserted, the damage would be irreversible. (Researchers presume that the damage seen in these previous studies may have been due to the use of older, less sophisticated imaging techniques.)

“For us to even see veterans for hearing loss,” said Oghalai, a scientist and clinician who treats patients in the Stanford Hospital & Clinics and directs the hearing center at Lucille Packard Children’s Hospital.

The increasingly common use of improvised explosive devices, IEDs, around the world provided the impetus for the new study, which was primarily funded by the Department of Defense. Among veterans with service-connected disabilities, tinnitus — a constant ringing in the ears — is the most prevalent problem, and hearing loss is the second-most-prevalent condition. But the results of the study would prove true for anyone who is exposed to loud blasts from other sources, such as jet engines, car air bags or gunfire.

More than 60 percent of U.S. service members who have been wounded in action have eardrum injuries, tinnitus or hearing loss, or some combination of these, and nearly 100 percent of all military personnel experience some degree of hearing loss post-deployment. The most devastating effect of blast injury to the ear is permanent hearing loss due to trauma to the cochlea. But exactly how this damage is caused has not been well understood.

“The ears are extremely fragile instruments. Sound waves enter the ear, causing the eardrums to vibrate. These vibrations get sent to the cochlea in the inner ear, where fluid carries them to tiny hair cells that are the auditory nerve fibers. These impulses are then sent to the brain via the auditory nerve, where they get interpreted as sounds.”

Permanent hearing loss from loud noise begins at about 85 decibels, typical of a hair dryer or a food blender. IEDs have noise levels approaching 170 decibels.

Damage to the eardrum is known to be common after large blasts, but this is easily detected during a clinical exam and usually can heal itself — or is surgically repairable — and is thus not typically the cause of long-term hearing loss.

“The answer to determining exactly what is causing the permanent hearing loss, Stanford researchers created a mouse model to study the effects of noise blasts on the ear.”

After exposing anesthetized mice to loud blasts, researchers examined the inner workings of the mouse’s hearing mechanism in the cochlea. The ears were examined from day one through three months. A micro-CT scanner was used to image the workings of the ear after destruction of the outer ear.

“When we looked inside the cochlea, we saw the hair-cell loss and auditory nerve-cell loss,” Oghalai said. “With one loud blast, you lose a huge number of these cells. What’s nice is that the hair cells and nerve cells are not immediately gone. The theory now is that the ear could be treated with certain medications right after the blast, that might limit the damage.”

Previous studies on larger animals had found that the cochlea was torn apart and shredded after exposure to a loud blast. Other scientists did not find this in the mouse model and speculate that the use of older research techniques may have caused the damage.

“We found that the blast trauma is similar to what we see from more lower noise exposures over time,” said Oghalai. “We lose the sensory hair cells that convert sound vibrations into electrical signals, and also the auditory nerve cells.”

Much of the resulting hearing loss after such blast damage to the ear is actually caused by the body’s immune response to the injured cells, Oghalai said. The creation of scar tissue to help heal the injury is a particular problem in the ear because the organ needs to vibrate to allow the hearing mechanism to work. Scar tissue damages that ability.

“There is going to be a window where we could stop whatever the body’s immune response would be right after the blast,” Oghalai said. “We might be able to stop the damage. This will determine future research.”

In addition to the Department of Defense, the study was funded by the National Institutes of Health and Chosun University in South Korea.

The first author of the study, Sung-II Cho, MD, assistant professor at Chosun University, was working at Stanford during the study. Other Stanford authors were graduate students Simon Gao, Jongmin Baek and David Jacobs; senior research scientist Anping Xia, MD, PhD; research technician Rosalie Wong; research associate Felipe Salles, PhD; computer programmer Patrick Raphael; and research coordinator Homer Abaya.

Woods Institute for the Environment awards seed grants to research projects

The Stanford Woods Institute for the Environment has awarded seed grants to three interdisciplinary research studies involving faculty in the School of Medicine and Department of Bioengineering, which is jointly supported by the medical school and School of Engineering.

The three studies are among seven environmental research projects chosen by a faculty committee led by two senior fellows at the institute. The projects will receive a total of $24,492 over two years to tackle a variety of environmental challenges.

Lead principal investigator MANU PRAKASH, PhD, assistant professor of bioengineering, and DAVID SCHNEIDER, PhD, associate professor of microbiology and immunology, will work on a project titled, “High Throughput Precision Measurement Tools for Insect-Parasite Ecology in Field Settings.”

STEPHEN LUBY, MD, professor of medicine, is principal investigator of a project titled “Lead-Contaminated Topsoil and Food in Rural Bangladesh.” His team members are Scott Fendt, PhD, professor of environmental earth system science; Pascale Dupas, PhD, assistant professor of economics; and Rosamond Naylor, PhD, professor of environmental earth system science.

MICHAEL HSIEH, MD, PhD, professor of radiology and pediatrics, will work on a project titled “Case of Schistosomiasis.” His team members are Giulio De Leo, PhD, professor of biology, and Susanne So-Kim, assistant professor of radiology.
vices, asking for a count of available beds for people in three categories: immediate (critically patients), delayed (serious injuries but not immediately life-threatening) and minor.

What response was, we have plenty of beds and staff. We can take as many as you need,” Weiss said. That call was the signal he was waiting for. At 12:05 p.m., he paged about 800 staff — including physicians, nurses, social workers, security officers and administrators — with a ‘code triage-stab’ message, indicative of an extraordinary situation that had risen that might call for additional manpower and supplies.

Weiss also dialed his partner in disaster response, Brandon Bond, administrative director of the Office of Emergency Management for Stanford and Packard hospitals. Bond, who had been at home in San Mateo, about to take his dog for a walk, immediately changed into work clothes and drove his truck to Stanford, calling the county emergency services on the way to monitoring information coming over public safety radio frequencies. The more he heard, the more he felt the signal he was waiting for. At 12:05 p.m., he called the county emergency services, asking for a count of available beds and supplies.

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“This told everyone ‘all hands on deck, expecting major casualties, open the command center, clear out the emergency department and deploy the caches of disaster equipment that had already been pulled out and pre-staged,” Bond said.

“Within 30 minutes we had admitted or discharged most of the patients who were previously being treated in the emergency department, and we mobilized over 150 health-care providers dedicated to responding to the airplane tragedy,” said Weiss, who is also an associate professor of emergency medicine at the School of Medicine. “This included physicians, nurses, technicians, clerks, registration personnel, transporters, social workers, translators and other vital specialists from throughout Stanford and Packard hospitals.

Teams set up a mass triage area in the emergency department parking lot and equipped and staffed a large area for less-urgent casualties from the incident. At that point, seven trauma teams consisting of physicians, surgeons, nurses, technicians, radiologists and scribes were ready to receive patients. We were set up to see more patients than we initially saw. Thanks to the incredible response from both hospitals, we could have probably cared for twice as many patients,” Weiss said.

David Spain, MD, chief of trauma and critical care surgery, was already on site when patients began arriving. After the helicopter arrived came ambulances carrying three or four patients at a time. The final seven patients arrived in a SamTrans bus.

By the end of the day, close to 200 people injured in the crash were treated at the hospitals.

An ambulance carrying crash victims arrives at Stanford. Fifty-five were treated at the medical center.

By Rosanne Spector

It’s right before your eyes: The water you drink, the air you breathe, your neighborhood — in other words, your environment — can make or break your health.

This simple truth gnawed at Pulitzer Prize-winning reporter Shirk Fink as he wrestled with how to cover Hurricane Sandy last fall. As she writes in the new issue of Stanford Medicine magazine, “The images of the hurricane spiralling toward my city, and the knowledge that thousands of New York’s most fragile residents would be left in its path, in facilities that were not hardened to withstand such a storm, was a potent outrage, made my stomach sink.”

Fink’s article on heroes in New York City in the nick of time for centenarian Winifred ‘Buzz’ Thompson, PhD, co-director of the Woods Institute for the Environment, “The images of the hurricane spiralling toward my city, and the knowledge that thousands of New York’s most fragile residents would be left in its path, in facilities that were not hardened to withstand such a storm, was a potent outrage, made my stomach sink.”

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The magazine is available online at http://stanmed.stanford.edu. Print copies are available for $7.50 each. Others can request a copy at 723-6911 or by sending a check or money order to: Stanford Medicine, Comm and Marketing, 2217 University Avenue, Stanford, CA 94305.
Mouse model reveals a mystery of Duchenne muscular dystrophy

By Krista Conger

Children with Duchenne muscu-
lar dystrophy often die as young adults from heart failure and infections. However, scientists have puzzled for decades by the fact that laboratory mice bearing the same genetic mutation re-

sponsible for the disease in humans display only mild symptoms and no cardiac involvement.

Researchers at the School of Medicine have developed a mouse model that accurately mimics the course of the disease in children and young adults with the condition, said Helen Blau, PhD, the Donald E. and Delia B.

400,000 people in the United States and 6 million adults with the condition,“ said Helen Blau, who is also a member of the Stanford Institute for Stem Cell Biology and Regenerative Medicine and a profes-

found cardiac defects and die at a young age, Blau said.

In prior Down syndrome research, scientists have targeted beta-2 adrenergic receptors for treatment of the disorders. But it may be that treatment even earlier would have had a more marked effect.”

Mourkioti treated af-

nected by oxidative stress. The scientists saw improvement on a standard test of contextual learning in mice. In contextual learning, the brain integrates sensory and spatial information to not change their personalities or the way

aim is to enable these children to do better in school,” Salehi said. “It is absolutely not to change their personalities or the way they react to society.” Changing a child’s per-

mings also supported the work.

The new study refined this work by targeting only one group of receptors that respond to norepineph-

Because people with Down syndrome are

cantly have a mouse model with which norepinephrine

drug that activates the same receptors, Salehi said. The dose used in this study was many times higher than that used for asthma treatment, he cautioned, so it is not known whether it is safe. A lower dose might work, or other drugs that affect beta-2 adrenergic receptors might be safer and more effective in humans. Research-

The Department of Psychiatry and Behavioral Sciences also supported the work.

Mourkioti and Helen Blau are authors of the first-ever study to demonstrate a molecular basis for the cardiac defect that is the primary killer of people with Duchenne muscular dystrophy.

Drug improves cognition in mouse model of Down syndrome, scientists say

By Erin Digitale

An existing FDA-approved drug improves cognitive function in a mouse model of Down syndrome, ac-

children with Down syndrome often die as young adults. Theories to date have focused on muscular involvement. Duchenne muscular dystrophy is the most prevalent form of the heritable muscle diseases. It is caused by deletion or other changes of one copy of the dystrophin gene that

in the brain center used for spatial navigation, paying atten-

cates that the lack of the protein further exacerbates telomere shrinking — a fact borne out when the researchers com-

death was a consequence of the disease, the study said. It also showed how early intervention, which the brain inte-

Drug improvements in mouse model of Down syndrome take a step closer

By Ahmad Salehi

Down syndrome, which is caused by an extra copy of chromosome 21, results in both physical and cogni-

not to zero, early treatments have been shown to slow the progression of muscular involvement.

The Department of Psychiatry and Behavioral Sciences also supported the work.

The scientists saw improvement on a standard test of contextual learning in mice. In contextual learning, the brain integrates sensory and spatial information to

drug that improves cognition in mouse model of Down syndrome, scientists say

Enadrona. By Erin Digitale

An existing FDA-approved drug improves cognitive function in a mouse model of Down syndrome, ac-

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The vaccine continued from page 1

the vaccine. No adverse effects, serious or otherwise, that could be attributed to the trial vaccine were observed.

“We’re very excited by these results,” which suggest that the immunologist’s dream of shutting down just a single subset of dysfunctional immune cells without wrecking the whole immune system may be attainable,” said Lawrence Steinman, MD, professor of pediatrics and of neurology and neurological sciences at Stanford. Steinman is a renowned immunologist and multiple sclerosis specialist who treats patients at Lucile Packard Children’s Hospital. “This vaccine is a new concept. It’s shutting off a specific immune response, rather than turning on specific immune responses as conventional vaccines for, say, influenza or polio aim to do.”

The results must be confirmed in larger trials of longer duration, cautioned Steinman, who holds the George A. Zimmermann Professorship. To date, no DNA vaccine has ever been approved for human use, and any likelihood application is several years off. The vaccine’s observed beneficial effects began to drop off a few weeks after the 12-week vaccine-dosing schedule was discontinued.

Lawrence Steinman is a senior author of a study on the clinical results of a potential diabetes vaccine.

Clinical research training awards available through Spectrum

Applications are being accepted for two graduate-level award programs designed to advance the careers of the next generation of clinical and translational research leaders at Stanford:

• The KL2 Mentored Career Development Program provides senior fellows and junior faculty in health-related professions with financial support and advanced training in clinical and translational research. Award recipients will receive access to career-development mentors, tuition support and a salary subsidy. Research performed within the KL2 program is designed to help participants obtain future career opportunities in academic settings. The program is designed to help participants obtain future career opportunities in academic settings.

• The TL1 Predoctoral and Postdoctoral Research Training Program provides awards with partial tuition and stipend support for a fullyear of full-time instruction in clinical research methods. Recipients will have access to career-development mentors, tuition support and a stipend.

Both programs are managed by Spectrum, the Stanford Center for Clinical and Translational Science, a member of the Clinical and Translational Science Awards Network sponsored by the National Institutes of Health. For more information, visit the website or contact Anandi Krishnan, PhD, at anandi.krishnan@stanford.edu, or visit http://spectrum.stanford.edu.

Eight young scientists at Stanford, including three at the medical school, were selected to attend the 2013 Lindau Nobel Laureate Meeting at Lake Constance, in Germany.

The annual event brings together Nobel laureates and promising scientists from around the world to give a program of lectures, panel sessions, discussion sessions and master classes on chemistry, physics, or medicine and physiology. The meeting’s disciplinary focus alternates from year to year.

This year’s meeting, which focused on chemistry and was held from June 30 to July 5, involved 625 undergraduate students, graduate students and postdoctoral scholars from 78 countries, as well as 35 Nobel laureates, including two from Stanford: William Robinson, MD — professor and senior investigator at the Institute for Immunology, Transplantation and Infection. Roep found that levels of proinsulin-targeting CD8 cells — but not other CD8 cells or other types of immune cells in patients’ blood — were substantially depleted in patients getting doses of the vaccine, compared with those getting placebo injections.

“Individuals with preserved C-peptide are at lower risk of long-term eye, kidney and nerve complications,” said JDRF’s Insel. “So it’s intriguing that in this study, C-peptide levels were preserved or, at times, increased while patients were receiving the vaccine.” Although Insel wasn’t directly involved in the trial, JDRF helped to fund it and at one point held a royalty position in the vaccine. (Another funding source was the Laccia Foundation.)

The trial was sponsored by Bayhill Therapeutics, a company in which Steinman, along with Paul FJ. Uts, MD, and William Robinson, were minority shareholders and Joseph C. Yee, an MD student who was the principal associate professor of medicine, respectively — played a crucial role. The three Stanford faculty members shared senior authorship of the study with Hideki Gar, MD, CEO of now-dissolved Bayhill; Delmar Lloyd, president of the company; and Insel, who has since left the company.

The young researchers attending from Stanford were: Andrew Kruse, a PhD student in biochemistry; DaPhNe Che, a PhD student in structural biology; Ryosuke Iwashita, a PhD student in neurobiology; Timothy Kuc, a PhD student in cell biology and biology; Stephen Fried, a PhD student in physical chemistry; Shinya Maeda, a student in nuclear physics; Hidetsugu Kato, a PhD student in computer science; and ChiaYia PrasitDishide, a PhD student in pharmaceutical sciences.

The Department of Medicine and Department of Neurology and Neurological Sciences as supported this work.

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“Individuals with preserved C-peptide are at lower risk of long-term eye, kidney and nerve complications,” said JDRF’s Insel. “So it’s intriguing that in this study, C-peptide levels were preserved or, at times, increased while patients were receiving the vaccine.” Although Insel wasn’t directly involved in the trial, JDRF helped to fund it and at one point held a royalty position in the vaccine. (Another funding source was the Laccia Foundation.)

The trial was sponsored by Bayhill Therapeutics, a company in which Steinman, along with Paul FJ. Uts, MD, and William Robinson, were minority shareholders and Joseph C. Yee, an MD student who was the principal associate professor of medicine, respectively — played a crucial role. The three Stanford faculty members shared senior authorship of the study with Hideki Gar, MD, CEO of now-dissolved Bayhill; Delmar Lloyd, president of the company; and Insel, who has since left the company.

The young researchers attending from Stanford were: Andrew Kruse, a PhD student in biochemistry; DaPhNe Che, a PhD student in structural biology; Ryosuke Iwashita, a PhD student in neurobiology; Timothy Kuc, a PhD student in cell biology and biology; Stephen Fried, a PhD student in physical chemistry; Shinya Maeda, a student in nuclear physics; Hidetsugu Kato, a PhD student in computer science; and ChiaYia PrasitDishide, a PhD student in pharmaceutical sciences.

The Department of Medicine and Department of Neurology and Neurological Sciences as supported this work.

Eight young scientists at Stanford, including three at the medical school, were selected to attend the 63rd Lindau Nobel Laureate Meeting in Germany.

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Sex

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with more grandchildren. The process is believed to be largely influenced by the male red deer, Garner said.

"You can think of this as being girl power at work in the animal kingdom," he said. "We like to think of reproduction as being all about the males competing for females, with females dutifully picking the winner. But in reality females have much more invested than males do, in terms of both their lifetime effort and what will interest the most. The sperm are just really jaws in a game that plays out over generations."

The study builds on a classic theory first proposed in a 1973 paper by scientists Robert Trivers and David Willard, founders of the field of evolutionary sociobiology. The hypothesis assumed that the determination of sex in mammals is random, with parents investing equally in their offspring to generate a 50-50 sex ratio in the population. Instead, they hypothesized that mammals are selfish creatures, manipulating the sex of their offspring in order to maximize their own reproductive success. Thus, parents in good condition, based on health, size, dominance or other traits, would invest more in producing sons, whose inherited strength and bulk could help them better compete in the mating market, leading to a sex ratio more skewed toward sons, which is what appears in nature.

Traditionally, the sex ratio in mammalian populations has been attributed to the random determination of sex in males, with females investing equally in the offspring of either sex. However, recent studies have shown that males can manipulate the sex ratio to their advantage through various strategies, such as the production of more sperm or the selection of the sex of the offspring.

"We are strongly advising faculty to register so they will be notified if their data are ready to be reviewed and can make sure the information is accurate and, if need be, engage in the dispute-resolution process," said Kathy Gilliam, director of the university's conflict-of-interest program.

It will be up to individual faculty members to monitor the data reported on payments to them and, as needed, to work with the Center to correct what they believe may be faulty figures. Physicians will have the opportunity to appeal the data in question to the second quarter of 2014. The law does not apply to medical residents. Kendra Marettle, deputy vice president of strategic operations at the Pharmaceutical Research and Manufacturers Association, said companies are scaling up, in some cases doubling their efforts, to comply with the law. As part of the association's recommendations to the Centers for Medicare and Medicaid Services, companies would identify a point of contact with physicians and hospitals who could turn to for questions and dispute resolution.

Harry Greenberg

Sunshine

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permitted at the medical school. I hope the database makes the reasons for specific payments clear and that the data are presented in a searchable manner. There is potential, given the massive amount of complex data, that there will be errors. But the new system is part of a larger movement nationwide toward greater transparency in physician-industry relationships. Several states, including Maine, Massachusetts, Minnesota and Vermont, already require public reporting of these financial relationships. And some companies have already voluntarily disclosed physician payments on their own public websites in anticipation of the new law.

The School of Medicine now publicly discloses information on faculty consulting relationships with industry in the academic profiles on its website (http://med.stanford.edu/profiles). If a faculty member received payments on their own public websites in anticipation of the new sunshine law, the School of Medicine now publicly discloses information on what institution received the funding, how much money was involved and whether the consulting relationship was publicly disclosed.

The first reporting cycle includes only five months of 2013, and continuing through Dec. 31. This data will form the base record of three generations. Major mammal groups were divided into males and females, with sons and sex traits included. The hypotheses make similar predictions — that females would choose mates with particularly "good genes" (e.g., for attractiveness) should produce so-called "sexy sons" as a result.

The hypothesis was reinforced in 1984 in a seminal Nature paper by T.H. Clutton-Brock at the University of Cambridge, who found that among wild red deer, females who produced more sons also gained more grandchildren from those sons. In fact, this key prediction of the hypothesis has remained untested, because complete third-generation pedigrees are so hard to obtain in the wild, Garner said.

Yet Garner and his colleagues were able to advance the research by reconstructing three-generation pedigrees of multiple species. They turned to the San Diego Zoo and biologist Greg Vicino in combing through decades of records on more than 38,000 animals from 678 species. The project was labor-intensive, requiring years of work to reconstruct the pedigrees and breeding histories of the animals, Garner said.

The researchers ended up with a pool of 1,627 granddams (female grandparents) and 703 grandfathers (male grandparents) for whom they had a complete record of three generations. Major mammal groups were divided into males and females, with sons and sex traits included. The hypotheses make similar predictions — that females would choose mates with particularly "good genes" (e.g., for attractiveness) should produce so-called "sexy sons" as a result.

The same was true of granddams, with the researchers finding that when grandfathers produced mostly sons, those sons had 2.7 times more children per capita than those whose fathers bore equal numbers of male and female offspring.

"The question is, within each species, among females who had more sons, did those sons do better in terms of producing more grandchildren per capita? And the answer is yes," Garner said. "Females are choosing and being very Machiavellian about it. They're doing it for their own benefit."

Garner said there may be some parallels among hum- ans, with some women choosing mates based on the potential for reproductive success, or what some researchers would describe as being able to adjust their sex-ratios in response to social cues. For instance, in polycyamous societies, the top-ranking wife is in much better shape than the lower-ranking wife (the son holds the economic power in the family). And a study of 400 U.S. billionaires, published in 2013, found that they were more likely to have sons than daughters — presumably, the scientists hypothe- sized, because sons tend to retain the family's wealth.

Garner's personal favorite is a study published in 1988. It found that mothers with an inherited speech disorder had three times as many sons as daughters, in theory because a son with a speech impediment would be at a disadvantage when it came to a marriage or a court- paired daughter, whose success is more dependent on speech and social skills, Garner said.

Garner said his study emphasizes the huge research potential of zoo data. "The temptation might be to assume that data from captive animals in the zoo has inherent problems," he said. For instance, zoo animals are more likely to be older, with more experience to select mates. Moreover, females in the wild rely on environ- mental cues to tell them to produce sons or daughters, whereas in captivity may be misleading among animals in captivity, he said.

"You would think that all of these conditions would have a ruinous effect, but it turns out that the zoo can be a case study of manipulating sex ratios, and it would appear to be beneficial for the environment," Greenberg said.

And there is a lot room for error. For instance, on a recent pharmaceutical website, a faculty member was re- ported as having received a $372,000 honorarium from a company, while the records showed they worked primarily in research in which the physician served as principal investigator, Gar- mill said.

There are other potential pitfalls in the system. For instance, the industry-related data in the school's academic profiles is posted on a different time schedule than the data in the new system, so there will likely be discrepancies between the two, raising poten- tial questions.

"We are trying to do everything we can to make sure there isn't this disparity, but I also encourage faculty to look because the me- dia and other groups will also be instigating," Greenberg said.

There has been speculation that disclosure of indus- try-related data may lead to changes in physician behavior, including their drug-prescribing habits. Some might choose to avoid industry connections altogether because of worries about patient and peer backlash or because of worries about patient backlash or because of worried about patient backlash. Greenberg said her concern is that the new sunshine law will lead to greater transparency in the industry's interactions with physicians. She said it is also important for physicians to update their profiles in the National Provider Plan and Enu- meration System database, a registry of health-care providers, to make sure they are up-to-date and that they include their public websites or any other related activity.

"We are strongly advising faculty to register so they will be notified if their data are ready to be reviewed and can make sure the information is accurate and, if need be, engage in the dispute-resolution process," said Kathy Gilliam, director of the university's conflict-of-inter- ests program.

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"You would think that all of these conditions would have a ruinous effect, but it turns out that the zoo can be a case study of manipulating sex ratios, and it would appear to be beneficial for the environment," Greenberg said. "I think this situation has the potential to be very interesting."
Two moms, and a whole lot of care, save young girl’s life

By Winter Johnson

For Arica Stiltha and Leanne Jones, it would be tough, if not impossible, to ever have a baby.

Arica had endometriosis, a condition in which tissue that lines the uterus develops outside it, often causing infertility. Leanne had uterine cancer. So the Chico, Calif., couple made a loving commitment to adopt soon-to-be born Davan Jones, even though they were both prior to birth that Davan would face huge medical problems.

Davan’s birth and adoption in December 2011, has spent more than 75 percent of her life at Lucile Packard Children’s Hospital, which is known for taking on some of the toughest pediatric cases in America. The problems Davan faced were beyond scary; three holes in her heart, a left vertebricle obstruction, abnormal pulmonary and mitral valves, a narrowing of her aorta, plus a life-threatening liver condition called biliary atresia. Despite the challenges to their child’s health, the couple said Davan was “destined” to be theirs.

Davan, whom her parents say is a superhero, has been on quite a rollercoaster ride since birth. When she was 3 weeks old, Packard Children’s surgery team recommended a procedure to help correct the bile duct deformity and intestinal problems caused by biliary atresia. But that was only step one of the multidisciplinary and aggressive strategy used to care for Davan.

Cardiologist Sharon Chen, MD, was hoping Davan could gain weight prior to fixing her multiple heart problems, but her heart could no longer wait to be repaired. In June 2012, cardiothoracic surgeon M. Todd Field, MD, was renowned for fixing the smallest of hearts all over the world, deliberately repaired the end-stage problems in 6-month-old Davan’s heart. Recently, Davan has undergone her third surgery for fixing the smallest of hearts all over the world. Davan is now home and getting well.

There is some concern that the risk of rejection is slightly higher when you cross blood types, but we have had great success with this type of transplant in our younger population,” said Hurwitz, noting that Packard Children’s has performed more than 20 such living donor transplants in children less than 4 years old. Young children’s immature immune systems appear less prone to reject a liver from a parent, compared to a matched blood type, and the Packard Children’s team also tailors the child’s immune-suppressing drugs to avoid immunological problems

In December 2012, Davan’s liver was still in trouble. The team decided to use a donor organ that did not match Davan’s ABO blood type, a step that many other hospitals avoid. “There is some concern that the risk of rejection is slightly higher when you cross blood types, but we have had great success with this type of transplant in our younger population,” said Hurwitz, noting that Packard Children’s has performed more than 20 such living donor transplants in children less than 4 years old. Young children’s immature immune systems appear less prone to reject a liver from a parent, compared to a matched blood type, and the Packard Children’s team also tailors the child’s immune-suppressing drugs to avoid immunological problems.

In April 2012, Davan’s mother was told the liver was ready for transplant surgery. A gift of organ donation: “This donor gave our child life. Making sure Davan takes her daily medication fulfills this donor’s gift.” Arica said.

While Davan is not able to utter whole sentences yet — only happy squeals — her mothers have become her voice: “We believe there are no coincidences in life,” said Arica about her daughter’s life. “Arica and I got the best gift ever in Davan, and we will always be thankful to everyone on the team at Packard Children’s for ensuring we’d be able to take her home.”

Winter Johnson is a media relations manager at Lucile Packard Children’s Hospital.