Study says aspirin lowers melanoma risk in women
By Elizabeth Devitt

In the largest study ever to explore new ways to prevent melanoma, researchers at the School of Medicine have discovered that women who took aspirin on a regular basis had a reduced risk of developing this skin cancer. Results also showed that the longer women took aspirin, the lower their risk.

The study was published online today in the journal Cancer.

The data for the study were drawn from the Women’s Health Initiative, a broad demographic of postmenopausal U.S. women ages 50-79 who volunteered to provide information about their lives — such as diet, activity, sun exposure history and medication — for an average of 12 years to help researchers understand factors that may affect the development of cancer and other diseases.

The Stanford study focused on the data of roughly 60,000 Caucasian women who were selected because less skin pigment is a risk factor for melanoma. The Stanford study's lead author. The researchers found that at a population level there are additional factors that contribute to diabetes risk besides obesity and total calorie intake, and that sugar appears to play a prominent role.

Specifically, more sugar was associated with an increased risk of diabetes, with a greater than 30% increase in risk for those who consumed the most sugar.

The study was published March 6 in the journal of the American Medical Informatics Association. The goal of this and previous research is to find fast, accurate methods of determining when a drug or combination of drugs cause unexpected side effects in some patients. The U.S. Food and Drug Administration encourages physicians to report any possible side effects through the agency's Adverse Event Reporting System. Such reporting is voluntary, however, and relies on a patient or a physician noticing that something unusual has happened.

Altmann's lab group had previously studied whether it was possible to comb through data from FDA reports to discover drug-drug interactions in an automated way. Using their data-mining methods on the FDA reports, the group reported in May 2011 that it had found a never-before-reported side effect of combining paroxetine, an anti-depressant medication, and pravastatin, a cholesterol-lowering drug. When a patient was taking both paroxetine (marketed as Paxil) and pravastatin (marketed as Pravachol or Selektine), the researchers found that the patient’s risk of developing hyperglycemia — high levels of blood glucose — was greater than the risk of hyperglycemia from taking either drug individually.

Web reveals unreported side effects of drugs
By Sarah C.P. Williams

Researchers at the School of Medicine and Microsoft Research have revealed that the Internet search history of consumers can yield information on the unreported side effects of drugs and drug combinations.

By analyzing 12 months of search history from 6 million Internet users who consented to share anonymized logs of their Web searches for research purposes, the team was able to pinpoint an interaction between two drugs that was unknown at the time of data collection.

“Seeking health information is a major use of the Internet now,” said co-author Nigam Shah and Russ Altman, along with other researchers, found that Web searches can yield information on unreported side effects of drugs.

Sugar quantity in food supply linked to diabetes rates, new study finds
By Erin Digitale

Does eating too much sugar cause diabetes? For years, scientists have said “not exactly.” Eating too much of any food, including sugar, can cause you to gain weight; it’s the resulting obesity that predisposes people to diabetes, according to the prevailing theory.

But now the results of a large epidemiological study suggest sugar may also have a direct, independent link to diabetes. Researchers from the School of Medicine, UC-Berkeley and UC-San Francisco examined data on sugar availability and diabetes rates from 175 countries over the past decade. After accounting for obesity and a large array of other factors, the researchers found that increased sugar in a population’s food supply was linked to higher diabetes rates, independent of obesity rates. Their study was published Feb. 27 in PLOS ONE.

“It was quite a surprise,” said Sanjay Basu, MD, PhD, an assistant professor of medicine at Stanford and the study’s lead author. The research was conducted while Basu was a medical resident at UCSF.

The study provides the first large-scale, population-based evidence for the idea that not all calories are equal from a diabetes-risk standpoint, Basu said. “We’re not diminishing the importance of obesity at all, but these data suggest that at a population level there are additional factors that contribute to diabetes risk besides obesity and total calorie intake, and that sugar appears to play a prominent role.”

Specifically, more sugar was linked to increases in diabetes rates.

Ten-year-old Mary Lisanti’s legs are now about even in length, thanks to surgeon Scott Hoffinger.

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Anthony Oro (right) and Scott Abwood (left) found a second method of blocking the Hedgehog pathway, which is abnormally active in a common type of skin cancer. The discovery may lead to more effective treatments for tumors that become resistant to an existing medication.

Discovery could pave way to better skin cancer therapy

By Krista Conger

Hailed as a major step forward in the effort to develop targeted cancer therapies, a recently approved drug for the most common type of skin cancer has been a mixed blessing for patients. Although the initial response is usually dramatic, the tumors often recur as the cancer becomes resistant to treatment.

Now researchers at the School of Medicine have identified a second way to block the activity of the signaling cascade, called the Hedgehog pathway, which is abnormally active in these cancers. The researchers hope the new approach may not only one day help patients with tumors that have become resistant to the first drug, vismodegib (marketed as Erivedge), but may also provide a novel combination therapy for newly diagnosed tumors that may be more effective than either treatment alone.

“These new, highly targeted therapies work really well,” said dermatology professor Anthony Oro, MD, PhD, who was one of several Stanford researchers involved in the multiyear effort that brought vismodegib to market in 2012. “But this type of treatment is a race against evolution. Within a year, many of the tumors recur when the cancers become resistant to the inhibitor.”

The effect on patients, particularly those with a severe condition called Gorlin syndrome, is a heartbreaking yo-yo as the tumors that cover most of their bodies disappear within weeks, but often recur in force.

But Oro and his colleagues’ discovery of another, previously unknown component of the Hedgehog pathway — a component vital...
Medical school stresses importance of computer encryption

By Ruthann Richter

A physician taking a red-eye flight to a conference on the East Coast straws her laptop in the airplane's over- head bin, then closes her eyes to get some rest. The next morning, she arrives at her hotel, suddenly realizing that she has left behind her laptop, containing detailed data on dozens of her patients.

She calls her medical center's information technology department in a panic. "Was the laptop en- crypted?" is the first question she is asked.

If so, the data will be scrambled — and completely unintelligible — to anyone who finds the laptop. Since thieves can't access the data on an encrypted computer or mobile device, the missing laptop essentially becomes a nonevent.

"That is why encryption is such a necessary thing in a health-care setting," said Michael Halaas, chief informa- tion officer for the School of Medicine. "Many other steps must be taken to protect data as well, but with encryption, the device is essentially brick if it is lost or stolen."

In this age of portable and dispersed data, a growing number of academic medical centers are looking to modern technology for computer encryption, which can be a complex undertaking requiring major institutional support.

"The university's policy is that all devices that store protected health information must be encrypted," Lowe said. "We are providing the technology and support to make sure we have full compliance with this policy and that encrypted data is indeed protected because the odds of it being stolen.

Incidents involving potential loss or exposure of protected health information have become increasingly common in recent years, with more than 543 reported incidents since 2010 of major breaches — those involving 500 or more individuals — at hospitals, health plans, clearinghouses and business partners, according to the Department of Health and Human Services. For example, last year Emory University Hospital, in Atlanta, reported the loss of 12 hard disk drives containing information on more than 315,000 surgery patients, including patient names, diagnoses and procedures, and in some cases So- cial Security numbers, according to the university. The VA also reported an increase in the number of VA facilities that lost or had data stolen or lost.

The largest-ever reported case involved the U.S. De- partment of Veterans Affairs, which reported the theft of 10 computer hard disks used to store information on 2.65 million veterans.

"People spend more time protecting their wallets than their devices," Halaas said. "But depending on what's in the device, the impact could be significant."

Incidents also may have consequences for the indi- vidual involved. At Stanford, for instance, a faculty or staff member who loses a device containing patient information, or data stolen, may be subjected to a serious correction action, depending on the circumstances, Cohen said.

However, the laptop or mobile device was en- crypted in accordance with federal standards, the inci- dent becomes a nonevent; no reporting is required, and the data remains secure. At Stanford, all encrypted de- vices are also backed up so that the critical data can later be retrieved and restored. There are strict policies in place to prevent unauthorized access to these backups. All requests to access a backup must first be reviewed and approved by the school's privacy officer, Lowe said.

He said contrary to some what, encrypting a computer does not make it slower, unstable or more difficult to access.

"These are no longer significant con- cerns with modern encryption technologies running on modern equipment," he said.

He said the technology is constantly evolving, with the time approaching when even with computers and mo- bile devices will be pre-encrypted before they hit store shelves.

"I believe that very soon that will be a standard fea- ture of computer technology," he said.

Clinical trial shows promise for novel anti-clotting drug

By Tracie White

An experimental drug has been shown to be significantly more effec- tive at preventing blood clots during coronary stenting procedures compared to the anti-clotting agent now typically used, according to an international, multicenter study whose senior author is at the School of Medicine.

Given intravenously, the novel anti- clotting drug, cangrelor, reduced the odds of complications from stenting procedures — primarily blood clots, but also heart attacks and strokes — by 22 percent when compared with the routinely used anti-platelet drug clopidog- rel, said the study, which was published online March 10 in the New England Journal of Medicine.

"We are pleased the trial delivered such clear results," said senior author Robert Harrington, MD, professor and chair of the Department of Medicine at Stanford. "This study examined a very wide spectrum of patients, which suggests the results likely ap- ply to a substantial percent- age of patients undergoing stenting procedures around the world."

Coronary artery stents are used in the majority of pa- tients who undergo percuta- neous coronary intervention, commonly called a "stent" procedure. (An esti- mated 600,000 are performed in the United States each year.) Interventional cardiologists perform PCI in the cath- eterization laboratory to reopen arteries in the heart that have become narrowed or blocked because of cardio- vascular disease, which af- fects an estimated 14 million Americans.

In order to prevent blood clotting during PCI, patients are routinely given oral doses of the anti-clotting agent clopidogrel (brand name Plavix). The drawback with this drug is that it is only available orally, which can make it difficult to adminis- ter if a patient is very sick. The drug is also slow to take effect, and it remains active for days after the procedure, said the Bhatt, MD, lead author of the study.

"We need a very potent agent to prevent clotting when we are put- ting a stent in the heart artery, like wires and stents, and Bhatt, a senior physician at Brigham and Women's Hospital, chief of cardiol- ogy at the VA Boston Healthcare System and professor of medicine at Harvard Medical School. "We want a fast-acting, reversible agent, which is why a drug like cangrelor could be useful and why we tested it."

The study, a randomized, double- blind phase-3 trial began in 2010, compared the use of intravenously ad- ministered cangrelor to orally admin- istered clopidogrel in about 11,000 PCI patients at 153 centers around the world.

"The use of cangrelor provided a re- duction in ischemic complications across the full spectrum of patients undergo- ing contemporary PCI, the study said. "The odds of having an ischemic event were reduced by 22 percent, and this benefit was not accompanied by any sig- nificant increase in bleeding or in transmural." Results did show increased minor bleeding in patients who had a PCI, but this was but to be expected because it is a more potent anti-clotting drug, and there was no in- crease in dangerous bleeding, the study said.

The trial was sponsored by the New Jersey-based pharmaceutical company, which makes cangrelor and plans to apply for U.S. Food and Drug Administration approval of the drug following the results of this trial, said Bhatt, also one of the other Stanford co-au- thors of the study.

Both Bhatt and Harrington reported receiving institutional research contracts from2011 INSIDE STANFORD MEDICINE
By Michelle L. Brandt

Cristianne Wijman, an expert in neurocritical care, dies

Cristianne (Christine) Wijman, MD, PhD, an associate professor of neurology and neuroscientist at Stanford Health Care, crossed over to the next life on March 8. TheDetails of her death were private.

Wijman was born in Amsterdam into a medical family (her father was a physician). She did her basic education in Amsterdam and received her medical degree from the University of Amsterdam in 1989. In 1997, she completed her residency in internal medicine in the Netherlands.

In 1999, Wijman received the European Board of Internal Medicine's Award for European Medical Graduates for a research paper on the clinical management of acute respiratory failure. In 2000, she accepted a position at Stanford Hospital & Clinics. "She helped us realize how important it was to act quickly to evaluate someone with cardiac arrest. At the time of her death, she was the national leader in research in the field of hypothermia for the treatment of stroke and other neurologic disorders. Furthering the understanding of these disorders and identifying new treatments is the work that I have devoted my career toward," said Thomas G. Steiner, MD, professor of neurology and neurosurgery.

"Cristanne will be missed in the stroke community and especially here at her Boston home, where she has many friends," said Carlos Kase, MD, neurologist in chief at Massachusetts General Hospital and member of the World Stroke Organization. "She was truly one of a kind," said Anna Finley Caulfield, MD, Stanford's first neurocritical care fellow and now an assistant clinical professor. "She was passionate about everything she touched on, she owned the room. It took me a whole day to get over the fact that this young woman with a Dutch accent was actually a neurologist.

Reflecting on applications in the field, Reitman said: "She achieved everything the set out to do." In addition to Reitman, Wijman is survived by her son, Fred; her daughter, Anna; her sister, Marjolein Vreeswijk-Scholten; and her brother, Gerrit-Jan Wijman. The family held a private memorial service on March 8.

Cristianne Wijman, an emeritus professor of medicine and neuroscientist at Stanford, died March 8. She was 54.

"She was very giving and generous with her knowledge, her time, her skill and her wisdom," said "Dr. Wijman was a leader in neurocritical care whose scholarly and clinical work have advanced the care of patients throughout the world," said Lloyd Minor, MD, dean of the School of Medicine. "Her passing is a great loss for the Stanford community, and we extend our heartfelt sympathy to her family," said Minor.

Wijman served as director of the neurocritical care program since its inception in 2001. There, she oversaw and trained colleagues on the care of critically ill patients in the intensive care unit with cerebrovascular and other neurologic disorders. Furthering the understanding of these disorders and identifying new treatments is the work that I have devoted my career toward," said Thomas G. Steiner, MD, professor of neurology and neurosurgery.

"She was a gifted teacher, whose trainees were immediately exposed to her larger-than-life personality. She never forgot meeting her," said Steven A. Ventresca, MD, chief of the department of emergency medicine at Stanford Hospital & Clinics. "She helped us realize how much could be done for people with devastating strokes or other neurologic illnesses, and she taught us how important it was to actively evaluate someone with sudden changes in condition."

In her specific research interests included the causes and optimal treatment of brain hemorrhages, the use of hypothermia for the treatment of stroke and brain injury, and the prediction of outcomes in critically ill patients. Wijman was a sought-after surgeon at cardiac arrest. At the time of her death, she was the principal investigator on several clinical trials. A 2009 Stanford Hospital article noted that her R01 grants "made her the only critical care neurologist in the U.S. with this level of NIH funding success.

"Wijman's work was extensive, having authored more than 75 scientific articles and more than 120 peer-reviewed abstracts. She was the recipient of numerous awards, including the 2006 H. J. Linsky Forno Award for Teaching Excellence given to her by Stanford neurology residents.

In 2009, Wijman received the IEEE Engineering with Standards award. She was known to be energetic and committed, both in her professional and personal life — someone who, her husband said, "lived for the fullest." The type of person to be the first on the dance floor, Wijman loved being part of the HyperTonic, a band she helped to put together, as well as part of several other Stan- ford neurologists. "I was always someone who loved to dance and sing, and I could keep the tune," Wijman told The New York Times.

"Wijman was the kind of person to be the first on the dance floor, Wijman loved being part of the HyperTonic, a band she helped to put together, as well as part of several other Stan- ford neurologists. "I was always someone who loved to dance and sing, and I could keep the tune," Wijman told The New York Times.

Karl Deisseroth receives Lounsbery, "Brain" awards

Karl Deisseroth, MD, PhD, professor of bioengineering and of psychiatry and behavioral sciences, has been named the recipient of two awards — the Grete Lundbeck European Brain Research Prize, also known as the "Brain Prize," and the Richard Lounsbery Award — for his work in optogenetics.

Deisseroth, who holds the D.H Chen Professorship, pioneered the technique in which neurons can be selectively activated or inhibited with pulses of light. It is a powerful tool for better understanding the brain's circuitry.

Deisseroth shares the Brain Prize, a neuroscience award worth 1 million euros, with five other researchers. There was no neurologist among the nominees. Deisseroth also received the Richard Lounsbery Award, which is given to "outstanding individuals in the biological sciences who are working early in their careers and have made significant contributions to our understanding of the brain."

Deisseroth's work in optogenetics has been recognized by multiple awards, including the 2013 National Academy of Sciences Award for Investigator. His laboratory, which is founded and directed by Deisseroth, is now located at Stanford University. In 2013, Deisseroth was awarded the Dreyfus Teacher-Scholar Award, which is given to the best young American and French scientist each year in recognition of extraordinary scientific achievement in biology and medicine.

Gordon Saul named executive director of Stanford Biodesign

Gordon Saul, MBA, has been appointed executive director of Stanford Biodesign and a consulting professor of bio- engineering. Biodesign provides medical technology innovation training to teams of doctors, engineers, and business students who identify a medical need, develop an invention to fill it, and create a plan for bringing the technology forward into patient care.

In his new role, Saul will manage the Coulter Translational Research Program in Bioengineering and the Spectrum medtech accelerator award, which provide seed grants for the development of devices, drugs and diagnostics to improve health care and lead to commercially available products. He will also establish and maintain connections with companies, federal and private foundations, and academic institutions that can participate in the biodesign community.

Saul has more than 20 years of experience in business development experience in the medical device and pharmaceutical area. He is an alumnus of the Stanford Graduate School of Business.
Researchers identify forerunners of cells that enable hearing

By Krista Conger

Researchers at the School of Medicine have identified a group of progenitor cells in the inner ear that can become the sensory hair cells and adjacent supporting cells that enable hearing. Studying these progenitor cells could someday lead to discoveries that help millions of Americans suffering from hearing loss due to damaged or impaired sensory hair cells.

“It’s well-known, in mammals, these specialized sensory cells don’t regenerate after damage,” said Alan Cheng, MD, assistant professor of otolaryngology. “In contrast, birds and fish are much better equipped. They can retain their sensory cells after trauma caused by noise or certain drugs.” Identifying the progenitor cells, and the cues that trigger them to become sensory cells, will allow us to better understand not just how the inner ear develops, but also how to devise new ways to treat hearing loss and deafness.

The research was published online Feb. 26 in Development.

Cheng is the senior author. Former medical student Taha Jan, MD, and postdoctoral scholar Renjie Chai, PhD, share lead authorship of the study. Roel Nusse, PhD, a professor of developmental biology, is a co-senior author of the research.

The inner ear is a highly specialized structure for gathering and transmitting vibrations in the air. The auditory compartment, called the cochlea, is a snail-shaped cavity that houses specialized cells with hair-like projections that sense vibration, much like seaweed waving in the ocean current. These hair cells are responsible for both hearing and balance, and are surrounded by supporting cells that are also critical for hearing.

Twenty percent of all Americans, and up to 33 percent of those ages 65-74, suffer from hearing loss. Hearing aids and, in severe cases, cochlear implants can be helpful for many people, but neither address the underlying cause: the loss of hair cells in the inner ear.

Cheng and his colleagues identified a class of cells called tympanic border cells that can give rise to hair cells and the cells that support them during a phase of cochlear maturation right after birth. “Until now, these cells have had no clear function,” said Cheng. “We used several techniques to define their behavior in cell culture dishes, as well as in mice. I hope these findings will lead to new areas of research to better understand how our ears develop and perhaps new ways to stimulate the regeneration of sensory cells in the cochlea.”

Cheng recently received a grant from the California Institute for Regenerative Medicine to study the limited regeneration of the same sensory hair cells that occur in a different region of the inner ear called the vestibular system, which helps us balance. Lessons learned there may also translate into aid for patients with hearing loss.

Although regeneration of sensory hair cells does not happen naturally, recent research has suggested that the mammalian ear may harbor a sub-population of — presumably inactive — progenitor cells. The research team led by Cheng and Nusse used a strain of laboratory mice that allowed the scientists to track the activation of a cell-signaling pathway driven by a protein called Wnt. The Wnt pathway has previously been shown to be involved in many developmental functions, and it drives the renewal and proliferation of many types of stem cells.

“We wanted to investigate the Wnt pathway because of its tremendous influence in the development and regeneration of many other organs,” said Cheng.

The researchers found that tympanic border cells, or TBCs, which form a thin layer under the sensory epithelium, are actively dividing in mice during the first three weeks after birth (the time corresponding to about the first trimester of human development, during which the ability to hear is established) and give rise to at least a subset of sensory and non-sensory cells in the ear. They also divided vigorously in isolated cultures when the Wnt pathway was activated, and stopped when the pathway was inhibited. Finally, the researchers showed that purified TBCs were able to specialize into hair cells and support cells when cultured in a lab dish.

“It’s surprising to think that these progenitor cells are among this largely underappreciated group of cells,” said Cheng. “This studyhighlights that, even in mice, there is a lot of maturation occurring after birth as hearing develops. This is really a story that needs to be understood. Next we’d like to look at these cells in models of hearing loss. Do they have the ability to regenerate? If so, under what conditions?”

Other Stanford researchers involved in the study include medical students Zahra Sayyid and Jared Levin; former postdoctoral scholars Renée van Amerongen, PhD, and Saku Sirkkonen, MD, PhD; senior research scientist Masahiko Aki, MD, PhD; postdoctoral scholars Tian Wang, MD, and Yi Arial Zeng, PhD; and professor of otolaryngology.

The research was funded by the Howard Hughes Medical Institute, the European Molecular Biology Organization, the Dutch Cancer Society, the National Institutes of Health, the American Otological Society, the Triological Society, and the Dutch Cancer Society, the National Institutes of Health, the American Otological Society, the Triological Society, and the Dutch Cancer Society.

Identifying how tympanic border cells become sensory hair cells could lead to discoveries that aid hearing loss.

10-year-old patient can finally get even, thanks to leg-lengthening surgery

By Robert Dicks

For the first time, Mary Lisanti’s legs are about even in length, thanks to a decade of care and planning by Scott Hoffinger, MD, an orthopedic surgeon at Lucile Packard Children’s Hospital.

Mary, 10, of Alameda was born with fibular hemimelia, which caused her left leg to be 3 inches shorter than her right. Hoffinger, an expert in treating the congenital bone deficiency, started laying the groundwork for such an operation while she was still a infant. She said everything would be fine, and he was right.

The main thing we do for kids like Mary is prevent contracture or loss of range of motion in the ankle of the shorter leg, Hoffinger explained. “We plan this through prosthetics and ankle-foot orthotics, thus allowing regular activities.”

True enough, said her mother, Lisa Lisanti. “There were no impositions,” he said. “Throughout childhood, Mary has been able to dance, play basketball and more.”

Hoffinger, who has successfully treated more than 50 leg-lengthening cases in his career, said that for kids like Mary, there is a point where prosthetics and orthotics cannot accommodate the entire difference. “So, in early 2012, the lengthening surgery began taking shape. “Dr. Hoffinger cares about the whole patient,” Lisanti said. “He felt Mary’s surgery would work better when she was older and could understand what was going on. Additionally, a larger percentage of the leg can be lengthened then.”

After some initial nervousness, the good-natured fourth-grader was on board. “Well, I always wondered what it would be like if my legs were more even,” she said.

To make it happen, Hoffinger had to break Mary’s tibia and fibula to allow surgical attachment of a Taylor Spatial Frame (a type of Ilizarov apparatus named after its Russian inventor) to her leg. This external fixator, composed of pins, wires and metal rings, allows daily turning of struts that in- duce a gradual, millimeter-size lengthening. “You can grow bone across the distraction gap,” Hoffinger explained. He monitored the ongoing lengthening for months in order to meet the approximate goal of 3 inches, which was achieved in October. “She’s about a centimeter shorter than the other leg,” he said.

Looking back at his daughter’s journey, Lisanti saluted Hoffinger’s technical proficiency, and his family-centered approach to Mary’s care. “Dr. Hoffinger is always very caring and concerned, and he creates the best possible atmosphere for two-way communication,” she said. “From the beginning, he always made our entire family part of the treatment process, and we think this played a major role in Mary’s success.”

Robert Dicks is the senior media relations director for Lucile Packard Children’s Hospital.
Sugar may play a more prominent role in the origins of diabetes than anyone realized, according to new research from Stanford, UC-Berkeley and UC-San Francisco (see story, page 1). Countries with more sugar in their food supplies have higher rates of diabetes, independent of sugar’s ties to obesity, other parts of the diet, and several economic and demographic factors, the researchers found.

Although the study focused on diabetes rates among adults, its results have repercussions for children’s health, too.

1 What do you think the findings mean for children’s health?

Robinson: Children’s behaviors and environmental exposure provide alternate explanations for the impact on adult health and disease. This study used sugar data for entire countries, not individuals. That means that both the children and the adults were living in countries where higher levels of sugars in the food supply were associated with higher rates of diabetes. The potential implications are even stronger for children than adults. Children are being exposed to that environment for a much longer time. This is particularly a problem in developing countries where their food supplies, diets and weights are changing so rapidly.

A number of us here at Stanford focus on what we can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only become apparent in adulthood. One can consider preventing diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can do in early life, and throughout the life span, to prevent diseases that have origins in childhood but only can disease risk.

2 What factors has prior research identified as the biggest contributors to the increase in diagnoses of type-2 diabetes in pediatric patients?

Robinson: The biggest contributor identified has been increased weight, but the increasing rate of type-2 diabetes among young and younger ages probably reflects obesity plus lots of different changes, including changes in our diets, such as more sugars and processed foods, and less physical activity. The CDC now projects that one in three U.S. children will have diabetes in their lifetimes, and it will be one in two among African-American and Latina girls. That is a pretty scary thought. That is why we focus so strongly on helping families improve their diets, increase activity levels and reduce sedentary time. We want to prevent and control excessive weight gain and all the problems that go with it, of which diabetes is just one.

3 In light of the new findings, do you think that parents whose children are not obese should be concerned about how sugar consumption could raise their children’s diabetes risk?

Robinson: This study doesn’t really address the question of what happens at the level of an individual child. However, it is still consistent with the advice we would give now, for both normal-weight and overweight children. I definitely recommend that parents try to reduce sugars in their children’s diets. Most parents are not even aware how much sugar their children are eating. Sure, sodas and sweets are the obvious sources, but sugars are also added to seemingly all processed foods, including even bread, pizza and French fries. The added sugars are just empty calories — providing extra calories and no additional nutritional benefit. So, I recommend that all parents try at least to reduce the obvious sources of sugary drinks, sweets and desserts.

4 What can we do to reduce children’s access to sugary foods? And are there any signs that we’re moving in the right direction on this issue?

Robinson: I think we are seeing evidence of moving in the right direction. Some recent data suggest that sugary drink consumption has dropped slightly. Unfortunately, sugar is in everything. Focusing on sugary drinks is probably the most promising approach. Parents are the policymakers for their own families, and they can be most effective by eliminating sugary drinks, including all sodas, fruit juices, sports drinks and energy drinks, from their homes. Policies to limit sugary beverages’ presence in schools and government buildings have also been successful at limiting consumption. We need a lot more of that.

5 What about putting a special tax on sugary drinks?

Robinson: Soda taxes are a promising strategy, although the beverage companies have successfully fought those by pouring in tons of money and misleading advertising. A recent survey found that the vast majority of Californians support soda taxes, especially if the money goes to health and obesity-prevention programs for children. The taxes proposed are minimal so far but, like for tobacco, taxes can help reduce demand by making sugary drinks more expensive and also help to offset, at least a little bit, the extra costs borne by society for extra medical and dental care, waste, pollution and even greenhouse gases associated with the production of sugary drinks.

Sugar continued from page 1

correlated with more diabetes: For every additional 150 calories of sugar available per person per day, the prevalence of diabetes in the population rose 1 percent, even after controlling for obesity, physical activity, other types of sugar, socioeconomic status and a number of economic and social variables. A 12-ounce can of soda contains about 150 calories of sugar. In contrast, an additional 150 calories of any type caused only a 0.1 percent increase in the population’s diabetes rate.

Not only was sugar availability correlated to diabetes risk, but the longer a population was exposed to excess sugars, the higher the diabetes rate after controlling for obesity and other factors. In addition, diabetes rates dropped over time when sugar availability dropped, independent of changes to consumption of other calories and physical activity or obesity rates.

The findings do not prove that sugar causes diabetes, Basu emphasized, but do provide real-world support for the body of previous laboratory and experimental trials that suggest sugar affects the liver and pancreas in ways that other types of foods or obesity do not. “We really put the data through a wringer in order to test it out,” Basu said.

The study used food-supply data from the United Nations Food and Agricultural Organization to estimate the availability of different foods in the 175 countries examined, as well as estimates from the International Diabetes Foundation on the prevalence of diabetes among 20- to 79-year-olds.

The researchers employed new statistical methods derived from econometrics to control for factors that could provide alternate explanations for their link between sugar and diabetes, including overweight and obesity; many non-sugar components of the food supply, such as fiber, fruit, meat, cereals and oils; total calories available per day; sedentary behavior; rates of economic development; household income; urbanization of the population; tobacco and alcohol use; and percentage of the population age 65 or older, since age is also associated with diabetes risk.

“Epidemiology cannot directly prove causation,” said Robert Lustig, MD, pediatric endocrinologist at UCSF Benioff Children’s Hospital and the senior author of the study. “But in medicine, we rely on the postulates of cause and effect. If you remove the sugar, the disease gets better; you re-expose and the disease gets worse again. This study satisfies those criteria, and places sugar front and center.”

“As far as I know, this is the first paper that has had data on the relationship of sugar consumption to diabetes,” said Marion Nestle, PhD, a professor of nutrition, food studies and public health at New York University who was not involved in the study. “This has been a source of controversy forever. It’s been very, very difficult to feed people large amounts of sugar to try to induce diabetes, scientists could put participants of a study on a low-sugar diet to see if it reduces diabetes risk.

Basu was cautious about possible policy implications of his work, stating that more evidence is needed before enacting widespread policies to lower sugar consumption.

However, Nestle pointed out that the findings are consistent with other studies that suggest people should cut back on sugar intake.

“How much circumstantial evidence do you need before you act?” she said. “At this point we have enough circumstantial evidence to cut back on their sugar a lot lower than it normally is.”

This study received no external funding.

Thomas Robinson, MD, a professor of pediatrics and of medicine at the School of Medicine, conducts research on childhood obesity and directs the Center for Healthy Weights at Lucile Packard Children’s Hospital. The next full story in the series will cover the role of sugars and diabetes, including specific sugars, such as high-fructose corn syrup or sucrose, and also to evaluate the influence of specific foods, such as soft drinks or processed foods.

Another important future step, he said, is to conduct randomized clinical trials that could confirm a cause-and-effect connection between sugar consumption and diabetes. Although it would be unethical to feed people large amounts of sugar to try to induce diabetes, scientists could put participants of a study on a low-sugar diet to see if it reduces diabetes risk.

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New online tool helps patients find Stanford clinical trials

By Kris Newby

Stanford Medicine has launched a new clinical trials directory to make it easier for patients to find Stanford’s clinical trials and to help researchers track new clinical trials designed to evaluate new drugs, devices and treatments for safety and efficacy.

“Nationwide, almost 40 percent of all clinical trials fail to meet their patient enrollment goals,” said Harry Greenberg, the medical school’s senior associate dean for research and the director of Spectrum, the Stanford Center for Clinical and Translational Education and Research. “This is a very unfortunate waste of research dollars and of the time of patients and volunteers engaged as research participants. This is why the creation of clinical trials recruitment tool will help Stanford researchers accelerate patient enrollment, therefore, it is more quickly and efficiently recruiting to complete more clinical trials and interventions.

The new tool saves researchers data entry time by automatically loading trials listings each night from the U.S. government’s clinical trials database, ClinicalTrials.gov.

In addition, investigators can contact researchers or individuals interested in participating by sending them the trial information, and researchers can choose to turn on the ClinicalTrials.gov identifier to make it easier to identify for patients.

“This is an extremely convenient and easy-to-use tool,” said Tang. “We and other researchers are trying to leverage real-time website analytics, helping to determine which medical search terms elicit the highest patient interest.

Tang and her colleagues hope that the site may become an easy-to-use, intuitive and affordable one-stop shop for clinical trials patients and their families. Patients can search for Stanford clinical trials online using keywords that match their treatment areas.

“Nationwide, almost 40 percent of all clinical trials fail to meet their patient enrollment goals,” said Greenberg. “For many respects, we ask that Stanford researchers and, if necessary, edit the imported trial description. If an investigator ‘accepts’ a trial, it appears in the clinical trials directory and his or her public-view CAP web page. In addition, investigators can easily contact researchers or participants by selecting the appropriate trial and contacting information for multicenter trials listings.

“Our job is to find a drug or agent that is readily available, safe and effective,” Tang said. “We and other researchers are trying to identify commonly used and available vitamins, supplements and drugs, such as aspirin and other NSAIDs, that may prevent melanoma.

"I believe patients are telling us lots of things about their own symptoms, and the next on a symptom or drug related to someone else in their household, for example. But even if the data are messy, they said, enough messy data is out there to pick up useful signals — those with no interactions also had an unusually high rate of hyperglycemia searches, which would lead researchers down dead ends if they pursued them. But the results also suggested that around 12 percent of users of searching for drug combinations knew to have any interactions also had an unusually high rate of hyperglycemia searches, which would lead researchers down dead ends if they pursued them.

"We do not want to waste the efforts of researchers who are developing new drugs, devices and treatments for safety and efficacy. This is an extremely convenient and easy-to-use tool,” said Tang. “We and other researchers are trying to leverage real-time website analytics, helping to determine which medical search terms elicit the highest patient interest.

Aspirin continued from page 1

researchers found that those who took aspirin decreased their risk of developing melanoma by an average of 21 percent.

Moreover, the protective effect increased over time: There was an 11 percent risk reduction at one year, a 22 percent risk reduction two years and as much as a 30 percent risk reduction at five years and beyond.

There’s a lot of excitement about this because aspirin has already been shown to have protective effects on cardiovascular disease and colorectal cancer in women,” said Jean Tang, MD, PhD, an associate professor of medicine at Stanford. She collaborated with Eric Horvitz, MD, PhD, distinguished scientist and fellow at Microsoft Research; and, mier Microsoft researcher Ryan White, PhD, who is the study’s lead author; and a colleague at Columbia University.

The MSN team developed automated tools for mining anonymized data from 82 million drug, condition and symptom searches performed by 6 million Internet users who had agreed, when they installed a Microsoft browser plugin, that the company could use their search history for research purposes.

White said the team used the automated tools to identify searches for information on paroxetine, provas- tatin or both during 2010. The tools then computed the likelihood that users in each group would also search for hyperglycemia and related terms of descriptors, such as “high blood sugar,” “blurred vision,” “frequent urination” or “dehydration.”

"We were really interested in gleaning from this data in a way that would help us understand long-term effects of NSAID users and nonusers of NSAIDs/dac helps reduce the risk of melanoma among women because aspirin and other NSAIDs, that may possibly play a more important role in strategies for preventing other kinds of cancer. The overall incidence of melanoma has been reported to be increasing, with the high- est risk in younger women and older men.

One way aspirin may prevent melano- noma is through its anti-inflammatory effects. Tang said. Even though non-aspir- in NSAIDs also reduce inflammation, they don’t use the same pathways that aspirin uses to become activated in the body. That difference may be the key to aspirin’s effectiveness.

Although the study results are prom- ising, Tang isn’t ready to declare a day will keep melanomas away. “We don’t know how much aspirin should be taken, or for how long, to be more effective,” she said. There are also downsides to aspirin use: Stomach complaints, ulcers and other side effects. However, she noted that 75 percent of women in the study were taking regular or extra-strength aspirin, not baby aspirin.

Aspirin continued from page 1

To test the accuracy of the search engine analysis, the team looked at 31 drug-drug interactions already known to cause hyperglycemia, and 31 interactions known to be safe. Overall, the drugs with known in- teractions led to more search queries on hyperglycemia. But the results also suggested that around 12 percent of users of searching for drug combinations knew to have any interactions also had an unusually high rate of hyperglycemia searches, which would lead researchers down dead ends if they pursued them. But the results also suggested that around 12 percent of users searching for drug combinations knew to have any interactions also had an unusually high rate of hyperglycemia searches, which would lead researchers down dead ends if they pursued them. But the results also suggested that around 12 percent of users searching for drug combinations knew to have any interactions also had an unusually high rate of hyperglycemia searches, which would lead researchers down dead ends if they pursued them. But the results also suggested that around 12 percent of users searching for drug combinations knew to have any interactions also had an unusually high rate of hyperglycemia searches, which would lead researchers down dead ends if they pursued them.
Healthy patients exemplify ‘indomitable nature of the human spirit’

By Erin Digitaile

Peter Hanson has survived a staggering array of medical challenges, including cardiac failure, a heart transplant, chronic ear infections, a broken leg, repeated bouts of pneumonia and a rare form of cancer.

Still, he leads the conventional line of an 8-year-old boy. He likes to play video games. He has friends and gets quantumly close to his classmates at Lucile Packard Children’s, who have assisted the Hanson family since they first walked through the hospital’s doors in 2005. More than any other family, the Hansons can appreciate Packard Children’s ability to handle complex patients. It has addressed not just Peter’s medical needs but also his family’s desire to be highly involved in his care, and Peter’s wish to be a regular kid.

Peter was born with a congenital heart defect. Soon after his second birthday, his heart began to fail. As he waited for a heart transplant, his condition became so dire that he was put in a medically induced coma.

“I remember at least one occasion where I had to resuscitate him doing chest compressions,” said David Cornfield, MD, chief of pulmonary and critical care medicine, who has cared for Peter during many of his stays in the hospital’s intensive care unit.

After several weeks, Peter’s liver began failing, too. His caregivers — from cardiology, intensive care, social work, nutrition and physical therapy specialization — gathered to tell his parents he might be too sick to receive a new heart.

“You’re pretty horrible,” to hear the news, said Peter’s mother, Katharine Hanson. “But it was great that all those people were there — people we had been relying on.”

“Nobody ducked that meeting,” Charles said, appreciatively. “Nobody said, ‘You tell em.’”

Fortunately, a last-minute dose of vitamin K (suggested by a fellow MD, then a fellow in the PICU) rescued Peter’s liver function. Two short days later, he received a new heart. The caregivers who had supported the Hansons at their worst moments helped them celebrate. In the hours before Peter’s transplant, Charles recalled, “it was a parade of nurses and doctors who had helped Peter coming to congratulate us and wish him well.”

The transplant, performed by cardiothoracic surgeon Bruce Reitz, MD, a professor emeritus of cardiothoracic surgery at the medical school, succeeded. As Peter recovered in the PICU, his mother and father were touched by the efforts that smoothed his recovery. The family became close to many of Peter’s nurses, respiratory therapists and child-life specialists, and to other children who had needed medical therapy and chemotherapy during Peter’s stay. It was a huge help in entertaining a restless 2-year-old in the pre-IPad era.

Peter left the PICU after 100 days. “For us personally, his challenges were far from over.”

After the long hospitalization, it seemed as though Peter would recover fully from this had happened; after an earlier surgical attempt to repair his heart defect, his family had needed another medical therapy and chemotherapy walk again. And it wasn’t the last, either: A few months after his heart transplant, when he had just re-learned walking for the second time, Peter was jumping on a trampoline and broke his leg. “So three times, Karen Kaufman and her colleagues in physical therapy taught him to walk,” Charles said.

Following Peter’s transplant, his new heart functioned well, but he developed many transplant medical problems. Frequent ear infections and bouts of pneumonia brought him to Packard Children’s otolaryngology and pulmonology teams.

Eventually, they diagnosed ciliary dyskinesia, a rare genetic disorder of the cilium that line the respiratory tract and help clear mucus from the lungs. The motion of Peter’s cilia was impaired, making it hard for his lungs to fend off infections even in the presence of vismodegib, which blocks a protein called Smo.

Fortunately, Packard Children’s is one of only a few designated ciliary dyskinesia centers in the country. And a pathology examination was further eased by the Hansons’ feeling that they had friends in every part of the hospital.

“I am in a group of Bartus family, and the prep waiting room is so fantastic,” Katharine said, citing one example of these important relationships. “She is such a warm, friendly person — she has got the right job.”

It is also a comfort to the Hansons to know that there are a whole lot of people behind the scenes,” Charles added. “We’ve met a lot of people who have saved his life many times, but we know there are many others who have helped him that we’ve never met.”

On Peter’s 8th birthday, in March 2012, he awoke in a pediatric ward. Instead of going to his birthday party, he began a series of assessments in Packard Children’s ophthalmology, neurology and oncology departments. Finally, his caregivers diagnosed cancer, a type of angioimmunoblastic T cell lymphoma never previously seen in a child. Peter spent the summer of 2012 receiving chemotherapy, an unusually complex endeavor, since he also takes immunosuppressants to keep his heart safe and anti-infection medications for his lungs.

“It was really necessary to make sure everyone worked hand-in-glove,” said Cornfield, who is also a professor of pulmonary medicine.

“We know that we are very fortunate to have Peter

Peter Hanson, shown here with parents Charles and Katharine Hanson, has benefited through the years from the complex-care expertise at Lucile Packard Children’s Hospital.

Now that we didn’t just draw the winning ticket in cardiology,” Charles added. “Because we have taken him to so many specialties, we know we don’t just hit the jackpot the first time.”

Charles and Katharine, who are both high school teachers, are also glad that their family’s caregivers are always learning from Peter.

Peter’s unusual medical situation has proved instructive for many Packard Children’s caregivers and researchers, Cornfield confirmed. But they’ve learned something more significant, too.

“The remarkable thing is that Peter is always a happy character, a real example of the indomitable nature of the human spirit,” Cornfield said. “That’s a lesson we could all learn from.”

Tumors

to its cancer-causing ability — could address this problem. Blocking the activity of this protein, called aPKC, can stop the growth in mice of transplanted skin tumors.

Researchers have become resistant to vismodegib, a drug that works through a protein called Smo. The finding, which was published in Nature last June described, is likely to bring new hope to cancer patients who had treated Peter coming to congratulate us and the Hansons’ feeling that they had friends in every part of the hospital.

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by John Sanford

It started with the Loch Ness Monster.

“So I drew Wilbur and Charlotte from ‘Charlotte’s Web.’ The spider dangled from a web inscribed with ‘Terroric Care.’” Pretty soon she was getting requests from colleagues. Her drawings got bigger and more complex.

“Peanuts” was the last I drew. I just started with something small — a little Loch Ness Monster,” she said. “I thought it would be cute, but I thought it would be erased the next day.”

A week later, it was still there. So Moceri, 28, erased it and drew something else. But she was worried someone might think she was wasting time. So she asked Myra Lang, the unit’s patient care manager, if it was OK. According to Moceri, Lang replied, “Yes, yes — I love it. Hey, can you draw me a little pig?”

So she drew Wilbur and Charlotte from ‘Charlotte’s Web.’ The spider dangled from a web inscribed with ‘Terroric Care.’

By John Sanford

Quick draw: Nurse’s artwork adds color to B2 unit

Alicia Moceri’s artwork adorns the whiteboard in the hospital’s cardiac-monitoring unit.

“Someone wants me to do the Sistine Chapel. I mean, really?”

“The pharmacist wanted Tom and Jerry.”

A request sheet was posted in the break room. It filled up fast. “Look, someone wants me to do the Sistine Chapel. I mean, really?” Moceri said, examining the sheet one day last fall. “Megatron and Optimus? Mary, who wrote here that you want Magic Mike?”

Mary Richards, an assistant patient care manager, rolled her eyes. “Oh, somebody’s horsing around.” Richards said.

“Good lord. I’m going to figure out whose handwriting that is.”

Moceri creates a new picture for the whiteboard every week. Other units have asked whether she can draw something on their whiteboards. “My unit has been joking that it’s going to hire me out and use the proceeds to fund a party,” she said.

Moceri said she has always liked to doodle and draw. Surprisingly, she does not have much formal training. “I had art classes in elementary and middle school, and I took an art class in high school and one in college,” she said.

The Redwood City native and resident earned a bachelor’s degree in nursing from San Jose State University. She has been a nurse at Stanford Hospital since 2008.

Patients have enjoyed her whiteboard drawings, and physical therapists have even encouraged her to draw for the patients who get out of bed, she said. “They say, ‘Hey, you need to go see what’s on the whiteboard.’”

Eugene Butcher named to endowed professorship

Eugene Butcher, MD, has been appointed the Klaus Bensch Professor in Pathology, effective Feb. 12. Butcher studies the trafficking of white blood cells, including their interactions with the endothelial lining of blood vessels, where they exit the circulatory system toward the site of tissue damage or infection, and their specialized chemotactic responses in tissues. A major focus of his research is understanding the physiologic significance and control of targeted leukocyte trafficking in human and mouse immunity and disease.

The professorship was established in 1999 by the Department of Pathology. It honors Klaus Bensch, MD, professor emeritus of pathology, who served as chair from 1986 to 1999. It supports a faculty member focused on basic and translational research in the field of experimental pathology.

Bensch’s primary research interests include identification of factors that control the proliferation and differentiation of human capillary endothelial cells and the elucidation of the role of genetic and environmental factors in cell aging.

Three researchers earn Pasarow Foundation Award

Three professors at the School of Medicine have been named recipients of the 25th annual Robert J. and Claire Pasarow Foundation Award, which includes a monetary prize of $20,000. Karl Deisseroth, MD, PhD, the D. H. Chen Professor in bioengineering and physiology, and his joint graduate students, Carla Schatz, PhD, the Sapp Family Provostial Professor in pathology, who served as chair from 1986 to 1999. It supports a faculty member focused on basic and translational research in the field of experimental pathology.

Bensch’s primary research interests include identification of factors that control the proliferation and differentiation of human capillary endothelial cells and the elucidation of the role of genetic and environmental factors in cell aging.

The award ceremony, which will be held May 10 in Los Angeles, is especially significant; it will be the final year the Pasarow Awards are given.

The foundation was established in 1987 to celebrate significant achievements in basic or clinical research, or both, with the key aim of increasing public awareness of critical disease areas such as cancer, heart disease and psychiatric disorders.