$90 million gift benefits cancer stem cell work

By Ruthann Richter

The School of Medicine has received $90 million from Ludwig Cancer Research on behalf of its founder, Daniel K. Ludwig, to support the school’s innovative work in cancer stem cells, which are believed to drive the growth of many cancers. Stanford is one of six institutions to share in a $540 million contribution to the field of cancer research from Ludwig. Announced Jan. 6, the gift is one of the largest ever made to the field from an individual donor.

The funding will augment the existing endowment for the Ludwig Center for Cancer Stem Cell Research and Medicine at Stanford, established in 2006, where scientists already have discovered some promising therapies that are moving into clinical trials.

“The gift from Ludwig Cancer Research is truly historic,” said University President John Hennessy, PhD. “Over the years, Ludwig has been an generous supporter of cancer research, and through its support changed the course of cancer treatment. But this extraordinary gift will spur innovation well into the future. Stanford is distinguished for its cancer research and has assembled a dream team of dedicated scientists at the Ludwig Center for Cancer Stem.” See LUDWIG, page 7

H1N1-triggered narcolepsy may stem from ‘molecular mimicry’

By Krista Conger

In a genetically susceptible people, narcolepsy can sometimes be triggered by a similarity between a region of a protein called hypocretin and a portion of a protein from the pandemic H1N1 virus, according to a new study by researchers at the School of Medicine.

The study provides some of the most compelling cellular and molecular evidence to date for a scientific concept known as “molecular mimicry.” Mimicry is the idea that the normal immune response to a pathogen, in this case the pandemic 2009 H1N1 influenza virus, can trigger autoimmunity — in which the immune system mistakenly attacks healthy components of the body — because of similarity between a pathogen protein and a human protein.

In a 2009 study, Stanford researchers reported evidence supporting the idea that narcolepsy, a debilitating disorder characterized by sudden, uncontrollable sleepiness and muscle weakness, occurs because the body’s immune system mistakenly destroys brain cells that make a “wakefulness” protein: hypocretin. The new study confirms that narcolepsy is an autoimmune disease.

“The relationship between H1N1 infection, vaccination and narcolepsy gave us some very interesting insight into possible causes of the condition,” said Emmanuel Mignot, MD, PhD, professor of psychiatry and behavioral sciences. “In particular, it strongly suggested to us that T cells of the immune system primed to attack H1N1” See NARCOLEPSY, page 6

Study: Staph can lurk deep within nose

By Bruce Goldman

Scientists at the School of Medicine have revealed that formerly overlooked sites deep inside the nose may be reservoirs for Staphylococcus aureus, a major bacterial cause of disease.

The results of their study were published Dec. 11 in Cell Host & Microbe.

The Stanford investigators further found that in bacterial species, Corynebacterium diphtheriae and Corynebacterium pseudodiphtheriticum, suggesting that the two organisms compete with each other and that C. pseudodiphtheriticum — or some molecular product it excretes — may prove useful in countering S. aureus infections.

“About one-third of all people are persistent S. aureus carriers and another third are occasional carriers and a remaining third don’t seem to carry S. aureus at all,” said David Relman, MD, the Thomas C. and Miling Yan, PhD, a graduate student in Relman’s lab at the time the experiments were performed.

“The nose has been long known to be a primary reservoir of S. aureus,” Relman said. The bug also abounds on the skin, with a special affinity for the armpits and groin. The vast majority of the time, however, it does little or no harm. (If it’s doing any good, no one has figured out yet what that is, Relman added.)

But if the skin is compromised by, for example, a wound or a medical incision or catheter placement, S. aureus can get into the bloodstream and cause serious and even life-threatening problems such as sepsis, pneumonia or infection of heart valves. Close to half of all S. aureus strains are resistant to a family of antibiotics that includes methicillin. In 2011, more than 80,000 severe methicillin-resistant S. aureus infections, as well as more than 11,000 related deaths, occurred in the United States alone, along with a much higher number of less-severe infections.

“Not everyone who carries S. aureus gets sick,” Relman said. “When they’re out walking the streets and otherwise healthy, attempts to rid them of their S. aureus are not necessary, and even sometimes futile. But once a carrier enters a hospital with an underlying illness or a weakened immune system or a high likelihood of undergoing skin-penetrating procedures, S. aureus carriage is a major liability.”

Rigorous and somewhat tedious regimens for placement, scientists find

By Bruce Goldman

Scientists at the School of Medicine have linked high testosterone levels in men to a poor immune response to an influenza vaccine.

In a study published online Dec. 23 in the Proceedings of the National Academy of Sciences, the investigators show that men with relatively high amounts of circulating testosterone benefit less, as measured by a boost in protective antibodies after vaccination against influenza, than do men with lower testosterone levels and women.

In men, high testosterone is linked to weakened immunity, scientists find

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Recovered bulimics poor at perceiving internal body cues, study finds

By Cynthia McKevey

Women who have recovered from bulimia nervosa have a difficult time perceiving their own heartbeats, according to a new study led by a researcher at the School of Medicine.

The ability to sense one’s own heartbeats and other internal body cues, such as hunger and fullness, is called interoception. Poor sensitivity to messages from the body might be related to the binge-purge cycle of bulimia, an eating disorder estimated to affect approximately 1.5 percent of the American population.

The gold standard for gauging interoception is the heartbeat detection task, in which a person — sitting in a chair without touching the backrest and with hands in lap — counts his or her heartbeats while being monitored on an electrocardiogram. A person with normal interoception will be able to track his or her own heartbeat with a certain degree of accuracy, though it probably will be difficult to do.

The study compared nine recovered bulimia nervosa patients to a control group of 10 people with no previous history of any sort of psychological disorder. The participants were women between the ages of 18 and 45. Those in the recovered bulimia nervosa group were significantly worse at accurately perceiving their own heartbeats than those in the control group.

On average, members of recovered bulimia group correctly perceived 46 percent of their own heartbeats, whereas members of the control group correctly perceived 64 percent.

The results were published in the December issue of Eating Behaviors. The lead author is Megan Klabunde, PhD, a postdoctoral scholar at the Stanford Center for Interdisciplinary Brain Sciences Research in the Department of Psychiatry and Behavioral Sciences.

A growing body of literature shows that heightened or suppressed interoception may be a contributor to or a prod-uc-t of many psychiatric disorders. For example, anxiety patients tend to be particularly sensitive to their own heartbeats, whereas people with eating disorders are less likely to accurately perceive their own heartbeat than those without anxiety.

Klabunde said it is the first study to use the heartbeat detection task to assess interoception in recovered bulimia nervosa patients. Klabunde said. Previous studies have involved participants to rate their own ability to detect hunger and satiety.

Klabunde said it is unclear whether diminished interoception results from structural abnormalities, a dysfunction of signals in the brain or something else. Klabunde wants to continue to study interoception in the context of eating disorders and in children who show a diminished ability to interpret their body’s signals. Klabunde is working on therapies that could help young people with poor interoception, including those with bulimia nervosa.

“The body is clearly involved in emotional processing,” Klabunde said. “We might have to be more creative in terms of dietary recommendations.”

Klabunde collaborated on the study with researchers at UC-San Diego and the Veterans Affairs San Diego Health Care System. The senior author is Walter K. Oei, MD, PhD, director of eating disorders programs at UCSD.

Klabunde said the study was supported by the National Institute of Mental Health.
**Study provides glimpse into health of ultramarathon runners**

By Molly Sharlach

For some runners, a marathon is not enough. Participation in so-called ultramarathons — defined as any distance beyond the standard 26.2-mile marathon — has grown exponentially in recent years. The number of ultrarunners who completed ultra-length races in North America increased from 15,500 in 1998 to 63,530 in 2012, according to UltraRunning Magazine. Despite its popularity, however, little is known about the health benefits or drawbacks of this extreme form of exercise.

To learn more about the health of ultrarunners, Eswar Krishnan, MD, assistant professor of medicine at the Stanford University School of Medicine, with Martin Hoff- man, MD, a professor of physical medicine and rehabilitation at UC-Davis and an avid ultrarunner. In November 2011 they launched the Ultrarunners Lon- gitudinal Tracking Study. Baseline findings of the study were published Jan. 8 in PLOS ONE.

More than 700 ultrarunners answered a web-based questionnaire about the competitions they entered and their training regimens, general health and running-related injuries over the previous 12 months. The re- searchers plan to follow this cohort of runners for 20 years.

Krishnan, a clinical epidemiologist, be- lieves that examining the effects of extreme exercise could have broader applicability. “It will help us to understand how much exercise is enough for health,” he said. “It’s a very important question.”

Not unexpectedly, baseline statistics in- dicate that ultrarunners are healthier than the overall U.S. population. During the previous year, study participants missed an average of just two days of work or school because of illness or injury, compared with four days for the gen- eral population of ultrarunners. Among their health professionals, about 64 percent, were for exercise-related injuries, not for diseases that would indicate chronic degeneration.

More than three-quarters of the ultrarunners re- ported an exercise-related injury in the prior year, while 65 percent had lost at least one training day to injury. Compared with the profiles of ultrarunners with those who had avoided injury revealed an interesting trend: Injuries appeared to be more common in younger, less experienced runners. It’s a bit like drivers. Young drivers are at higher risk of car crashes than older people. So similarly, peo- ple who have recently started running are much more likely to suffer injuries than veteran ultramarathoners,” Krishnan said.

With the next questionnaire, to be sent in early 2014, Krishnan and Hoffman hope to investigate whether particular knowledge or adaptations help to protect more experienced runners from injury. As in all runners, most injuries among study partici- pants involved the knees and other parts of the lower extremities. Notably, just 3.7 percent of injured ultra- runners reported stress fractures, small cracks in bones that can arise from repeated application of force over time. Stress fractures may be less frequent in ultrarun- ners than in other runners; studies have shown they make up 5 to 16 percent of all injuries in runners.

However, stress fractures in the foot appear to be especially common in this group, according to for 48 percent of all reported stress fractures. Hoffman and Krishnan speculate that running on uneven terrain may be the reason why.

Another striking, yet anticipated, finding was a high incidence of asthma and allergies. While only 7 to 8 percent of the overall U.S. population has each of these conditions, 11 percent of ultrarunners reported asthma and 25 percent reported allergies. The study authors believe that allergies may develop simply as a response to spending more time outdoors, or a contact with environmental pollen and other allergens. Krishnan expects that, as in marathon runners, most of the affected ultrarunners will be allergic to pollen, and he plans to follow up on this in subse- quent questionnaires.

Other valuable baseline findings from the study include statistics on hospitalizations after competitive ultramarathon events. Five percent of participants had been hospitalized in the prior year, and more than half of these injuries were report- ed due to dehydration, electrolyte disturbance or heat exhaustion. About 20 percent were for fracture or dislo- cation injuries. Krishnan hopes these findings can help improve the education of runners and medical person- nel about these dangers, but cautioned that falls during ultramarathons cannot be fully prevented.

The psychological profile of ultrarunners is of par- ticular interest to the researchers and will be a focus of the upcoming questionnaire. Krishnan and Hoffman are collaborating with several sports psychologists to conduct a study what drives these runners to such an extreme level of competition. “Understanding what motivates ultra- runners could be useful for encouraging others to meet minimum levels of exercise,” said Hoffman.

The study was supported by Veterans Affairs North- east Health Care Systems and the VA’s Endurance Run Foundation.

**Peter S. Kim**

By Bruce Goldman

Peter S. Kim, who for the past decade has served as president of Merck Re- search Laboratories, will join the School of Medicine this summer as a professor of biochemistry.

“I’m thrilled to come back to Stan- ford,” said Kim, 55, who received a PhD in biochemistry here in 1985. Kim, who will take up his position at Stanford on Feb. 1, also will be a member of the Institute of Chemical Biology and the Stanford Graduate School of Business.

The title, a joint venture of the School of Medicine, School of Engineering and School of Humani- ties & Sciences, brings together faculty interested in strengthening the chemical foundations of biomedical science.

“We in Stanford Medicine are simply delighted that Peter will be joining our faculty,” said Lloyd Minor, MD, dean of the School of Medicine. “With his many years as an innovative researcher and his extensive work in developing and shep- herding drugs to market, Peter exempli- fies our commitment to ensuring that the patients we see in our clinics ben- efit from the discoveries we make in our laboratories.”

“Peter’s kind of accomplishments as a structural biologist, mentor and captain of industry are legendary,” said chemistry professor Chaitan Khosla, PhD, direc- tor of the Institute of Chemical Biology and the Pritzker School of Molecular and Computational Biology. “He has made seminal contri- butions not only to the field of protein folding but also to our understanding of viral infection. What is perhaps most im- pressive about Peter is his restless spirit. I have every confidence that Peter’s greatest achievements lie ahead of him.”

Suzanne Pfeffer, PhD, professor and chair of biochemistry and the Emma Pfeffer Merner Professor of Medical Sci- ences, added: “I welcome a valued colleague of scientific and business credentials to Stanford.”

“We’re delighted that Peter has se- lected Stanford for the next chapter of his already remarkable career,” she said. “His experiences in industry will be invalu- able to our team as we focus on un- dustry and leadership will help cement the foundation of the new Chemical Biology Institute.”

During his 12 years at Merck Re- search Laboratories, the research-and-development hub of pharmaceutical giant Merck & Co., Kim led teams of chemists, biologists, engineers, statisti- cians and clinicians. Among the many products launched under his watch was a vaccine targeting human papilloma vi- rus, the causative agent of cervical cancer.

“Over a half-million women are di- agnosed every year with this terrible disease, which strikes them in the prime of their life,” Kim said. “After success- ful vaccination, the HPV vaccine, if we can distribute it broadly enough, could pre- vent up to 70 percent of these cancers.”

The day the HPV vaccine was approved, the “everybody in the company had an extra skip in their step,” he recalled. “It will help us to understand how much exercise to enhance health,” Hoff- man said.

Kim also oversaw the development of vaccines against rotavirus (responsible for more than 500,000 deaths annually worldwide) and against the reawakening of a long-dormant chicken pox infection in older or otherwise im- mune-compromised people. In addi- tion, drugs with novel mechanisms of action to treat Type 2 diabetes and the hepatitis C virus were introduced during his tenure.

“We saw some wonder- ful successes, together with some pretty visual fail- ures,” he said. “That comes with the game.”

At Stanford, Kim ini- tially pursued an MD/PhD through the university’s Medical Scientist Train- ing Program. As he became increasingly committed to research in biochemistry, he decided to forgo the two remaining years of clinical training for an MD. During his time at MIT, Kim un- covered a basic mechanism by which the influenza virus breaks into cells. As it turned out, this mechanism applies to a number of viruses, including HIV. Shifting his focus to the latter, Kim de- signed compounds that blocked the vi- rus from entering cells and began searching for an HIV vaccine based on similar principles.

In 2001, Kim was re- cruited to Merck Research Laboratories, where he ac- ceded to the top job in 2003. A decade of running the huge teams necessary for bringing a drug across the finish line has Kim well-prepared to learn to independent research. A self-declared optimist, he hopes to make progress on an HIV vaccine, which he called “the world’s most important unmet medical need.”

And he hopes to share his drug-develop- ment experience. “What I can bring to the table is an additional perspective that encompasses the pharmaceutical side of this equation,” he said. “It’s important that academic work that can be trans- lated does get translated. I’ll certainly be looking, at the institutional level, for ways to make it easier for individuals to navigate the translational pathway.”

The co-author of more than 150 peer- reviewed scientific articles, Kim holds 17 patents and is a fellow of the American Academy of Arts and Sciences and of the American Association for the Advance- ment of Science. He is also a member of the National Academy of Sciences and the Institute of Medicine.

“I have wonderful memories of Stan- ford,” Kim said. “I’ve seen up close the dramatic changes that have occurred since I was a graduate student here.” He is married and has three sons, all of whom are students at Stanford, he said.

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Clinical informatics recognized as subspecialty; nine physicians at medical center now certified

By Cynthia McKelvey

Much of what is known about sensory touch and hearing cells is based on indirect observation. Scientists know that these exceptionally tiny cells are sensitive to changes in size and pressure. But to truly understand how they function, scientists must be able to manipulate them directly.

Now, Stanford scientists are developing a set of tools that are small enough to stimulate an individual nerve or group of nerves, but also fast enough to mimic a realistic range of forces.

A team of Stanford ear specialists and mechanical engineers is developing a new device, known as a force probe, that allows the researchers to study the flexible hair bundles that are selected to mimic how the brain, scientists must be able to manipulate them directly.

Our ability to interpret sound is largely dependent on bundles of thousands of cells with hair-like projections on their surfaces. As sound waves vibrate the bundles, they force proteins in the cells’ surfaces to open and allow electrically charged molecules, called ions, to flow into the cells. The ions stimulate each hair cell, allowing it to transfer information from the sound wave to the brain.

Hear and other factors that contribute to the fine details of hearing loss because they do not know how to repair or replace a damaged hair cell. Physical manipulation of the cells is key to understanding the fine details of how they function.

This new probe is the first tool nimble enough to do it.

Bio-X researchers develop new technology to study hearing

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Researchers take step toward developing ‘universal’ flu vaccine

By Tom Abate

Every year, the approach of flu season sets off a medical guessing game, with life or death consequences.

There are many different strains of flu, and they vary from year to year. So sets off a medical guessing game, with authorities must make an educated guess and tell manufacturers which variants of the flu their vaccines should target.

Even when this system works, flu-related illnesses kill 3,000 to 49,000 Americans annually, according to the Centers for Disease Control and Prevention. A bad guess or the unexpected emergence of a virulent strain can send the death toll higher than expected.

Against this backdrop, Stanford researchers report promising steps toward the creation of a universal flu vaccine, one that could be produced more quickly and offer broader protection than the virus-specific inactivated available today.

The researchers detailed their work in a paper published online Dec. 16 in the Proceedings of the National Academy of Sciences. The senior author was James Swartz, D’Sc., the James H. Clark Pro- fessor in the School of Engineering and professor of chemical engineering and of bioengineering. The lead author was postdoctoral scholar Yuan Lu, PhD.

Their approach arises from a better understanding of the structure of a key protein on the surface of the flu virus, and a new process for making vaccines based on that understanding.

Protruding from the surface of the flu virus are hundreds of copies of a protein called hemagglutinin. Each copy of hemagglutinin resembles a mushroom, with a head and a stem. The head of hemagglutinin helps the virus enter and alter a host’s immune system, and the stem helps determine the virulence of a given strain of flu.

Today’s vaccines are based on inactivated viruses that contain the heads of hemagglutinin proteins. When a flu shot is injected into our bloodstream, our immune system sees the hemagglutinin head as a target and creates antibodies to fight what appears to be an infection.

Teaching the immune system to recognize a target is the essence of vaccination. If we are exposed to the flu after getting vaccinated, our immune system is primed to recognize and eradicate the invading virus before it can replicate sufficient copies to make us sick.

Swartz and his colleagues base their new vaccine approach on the understanding that, whereas the head of the flu virus varies from year to year, the protein stem remains more constant over time. Theoretically, a vaccine based on the stem should be more broadly protective against different strains of flu, and perhaps offer universal protection. Over time, because the stem remains relatively constant from year to year, our immune system produces antibodies against that antigen, multi-season protection might be possible.

But this approach remains experimental and has not yet been tested on patients.

The Stanford paper focused on the first step in developing such a universal vaccine: creating a protein stem fragment that could be injected into the bloodstream; in short, creating a target, or antigen, to attract the attention of the immune system and trigger an effective defense.

Lu, the lead author, outlined the process in detail in the PNAS paper.

He and the Stanford team used a relatively well-studied because it’s much more accessible — was the head of a protein in the flu virus. The head of hemagglutinin, or possibly a small molecule — is responsible for the death toll higher than expected.

The advantage of this process is that it can produce proteins in a few hours versus a couple of weeks or even a couple of months, which is how long it takes to make proteins for flu vaccines using the practices that are approved for medical use today.

The researchers used this process to create and refine a viral protein stem that would be useful as an experimental vaccine antigen.

It took dozens of tries over two years, but eventually the researchers fed a DNA snippet into the process and created a soluble viral stem protein that could be a good antigen. That is what they report in the PNAS paper.

Many steps remain before the research community knows whether this viral stem approach yields a better flu vaccine.

Next, Swartz and his team will attach their stem protein to a virus-like particle. The idea will be to create a bigger, better target with which to elicit an immune system response.

Should that prove successful, the new vaccine candidate would have to undergo safety and efficacy tests in animals and, eventually, large-scale human clinical trials.

Much is at stake. Recent estimates put the worldwide death toll from flu-related illnesses at between 250,000 and 500,000 persons per year.

“This is an important project for world health,” Swartz said, noting that the vaccine must not only be broadly effective against different strains of flu but cheap to produce so that it can be widely distributed. “These are big challenges but we are committed to the effort.”

The other co-author of the study was Stanford graduate student John Welsh.

The study was funded by the National Institutes of Health. Stanford’s Department of Chemical Engineering and Department of Bioengineering also supported the work.

Tom Abate is the associate director of communications at the School of Engineering.

Nose

bacteria repopulate those who are susceptible. The new study offers a possible reason why this is the case.

The scientists recruited 12 healthy subjects and brought them to a Stanford ear, nose and throat clinic run by Professor Peter Vautrin, MD, professor of otolaryngology. Employing special instrumentation to allow them to guide tiny swabs to precise locations within the nose, they took samples from three specific areas. The first location — and far and away the most well-studied because it’s much more accessible — was the anterior naris, a relatively dry skin-like patch of tissue located near the nostril. The second was the middle meatus — a warmer, wetter, mucus-producing fold found about midway up the nasal cavity. And the third was the sphenoethmoidal recess, situated deep within the cavity near the roof of the nose and, like the middle meatus, warm, wet and mucosal.

The researchers found that the presence or absence of S. aureus at one nasal site typically correlated with its presence or absence at the other two. An implication: If a person’s anterior naris is carrying the bacteria, the upper mucosal areas probably are, too. This could be why efforts to banish S. aureus have so often proved short-lived.

Focusing efforts largely on the bacteria in the anterior naris, which current decolonization procedures do, leaves deeper reservoirs intact.

Relman’s team learned three other things, as well.

First, the relative abundance of S. aureus was inversely related to that of another bacterial species, C. pseudodiphtheriticum. When one was present at high levels, the other was present at low levels or absent. One of the team’s co-associate professors, Pamp, PhD, a research associate in Relman’s lab, put the two bacterial species on an agar plate to scrutinize this relationship further, and found that C. pseudodiphtheriticum strongly blocked the growth of S. aureus.

The researchers suspect that something C. pseudodiphtheriticum produces and secretes — perhaps a protein, or possibly a small molecule — is responsible for S. aureus’ failure to thrive. If such a substance could be identified, Pamp said, it could provide clues to the development of new compounds to prevent or treat S. aureus infections.

Second, the microbial communities in those patients who harbor S. aureus differed in other ways from those in patients who don’t. This could mean that S. aureus alters its environment to make it more or less hospitable to various other microbes. Or it could mean that different microbial communities are more or less hospitable to colonization by S. aureus. If the latter is the case, it may be possible to predict, based on their resident nasal microbes, which patients are most likely to be at high risk of a S. aureus infection — even if they’re not currently carrying it — and monitor and treat them accordingly. Those patients found to be at lower risk could be spared such procedures.

Third, in the middle meatus and the sphenoethmoidal recess — the two deeper, wetter mucosal regions of the nose — microbial communities were similar to each other but quite distinct from the one inhabiting the more accessible and better-studied outer site, the anterior naris. This suggests that currently routine methods of sampling the nasal cavity for microbiology research purposes may be yielding skewed results.

Other study co-authors were graduate student Julia Fukayama, otolaryngology resident Do-Yoon, MD; and statistics professor Susan Holmes, PhD. The study was funded by a National Institutes of Health Pioneer Award, the Doris Duke Charitable Trust and the Thomas C. and Joan M. Merigan Endowment.

The Department of Microbiology and Immunology and the Department of Medicine also supported this work.
The poet Gwendolyn Brooks wrote that “every ending is the beginning of new things.” This is true in the field of stroke research when patients are given access to new therapies, technology, or research milestones. Our recent book gives readers a glimpse into a world patients rarely see: the emotional life of a physician. “All of us may not be physicians, or studying to be physicians, but we all have been patient,” said Audrey Shafer, MD, director of the program. “So a presentation like Dr. Ofri’s can be enlightening for both patient and practitioner.” The Arts, Humanities and Medicine Program regularly provides opportunities for workshops and educational opportunities for students and practicing healthcare practitioners to explore the self-knowledge and healing available through the expressive arts and other disciplines. Ofri, a neurologist with the Stanford community at 5:30 p.m. today at the Bing Concert Hall on the Stanford University campus. Her talk is titled “For Whom Do We Write?” A program, which is free and open to the public, is part of the Recombinations seminar series presented by the Arts, Humanities and Medicine Program at Stanford. The series is designed to bring students, faculty and staff together around topics at the intersection of the arts, medicine, humanities, science and technology. The book’s most recent book gives readers a glimpse into a world patients rarely see: the emotional life of a physician. “All of us may not be physicians, or studying to be physicians, but we all have been patient,” said Audrey Shafer, MD, director of the program. “So a presentation like Dr. Ofri’s can be enlightening for both patient and practitioner.” The Arts, Humanities and Medicine Program regularly provides opportunities for workshops and educational opportunities for students and practicing healthcare practitioners to explore the self-knowledge and healing available through the expressive arts and other disciplines. Ofri, a neurologist with the Stanford community at 5:30 p.m. today at the Bing Concert Hall on the Stanford University campus. Her talk is titled “For Whom Do We Write?” A program, which is free and open to the public, is part of the Recombinations seminar series presented by the Arts, Humanities and Medicine Program at Stanford. The series is designed to bring students, faculty and staff together around topics at the intersection of the arts, medicine, humanities, science and technology. Ofri’s most recent book gives readers a glimpse into a world patients rarely see: the emotional life of a physician. “All of us may not be physicians, or studying to be physicians, but we all have been patient,” said Audrey Shafer, MD, director of the program. “So a presentation like Dr. Ofri’s can be enlightening for both patient and practitioner.” The Arts, Humanities and Medicine Program regularly provides opportunities for workshops and educational opportunities for students and practicing healthcare practitioners to explore the self-knowledge and healing available through the expressive arts and other disciplines. Ofri, a neurologist with the Stanford community at 5:30 p.m. today at the Bing Concert Hall on the Stanford University campus. Her talk is titled “For Whom Do We Write?” A program, which is free and open to the public, is part of the Recombinations seminar series presented by the Arts, Humanities and Medicine Program at Stanford. The series is designed to bring students, faculty and staff together around topics at the intersection of the arts, medicine, humanities, science and technology. Ofri’s most recent book gives readers a glimpse into a world patients rarely see: the emotional life of a physician. “All of us may not be physicians, or studying to be physicians, but we all have been patient,” said Audrey Shafer, MD, director of the program. “So a presentation like Dr. Ofri’s can be enlightening for both patient and practitioner.” The Arts, Humanities and Medicine Program regularly provides opportunities for workshops and educational opportunities for students and practicing healthcare practitioners to explore the self-knowledge and healing available through the expressive arts and other disciplines. Ofri, a neurologist with the Stanford community at 5:30 p.m. today at the Bing Concert Hall on the Stanford University campus. Her talk is titled “For Whom Do We Write?” A program, which is free and open to the public, is part of the Recombinations seminar series presented by the Arts, Humanities and Medicine Program at Stanford. The series is designed to bring students, faculty and staff together around topics at the intersection of the arts, medicine, humanities, science and technology.

What Doctors Feel: an author to speak today at Clark Center

The Stanford research also was influenced by an unexpected finding in a study in China showed an increase in sudden-onset narcolepsy in children with the narcolepsy-associated protein HLA, which is found in about 20 percent of the population, to develop the disease.

Scandinavian, Chinese narcolepsy cases

The Stanford research also was influenced by an unexpected finding in a study in China showed an increase in sudden-onset narcolepsy in children with the narcolepsy-associated protein HLA, which is found in about 20 percent of the population, to develop the disease.

Surprisingly, we also found hypocretin cross-reactive T cells in blood samples from narcolepsy patients collected before 2009. This finding may provide a protective effect by giving the body the means to fight off an actual infection before cross-reactive T cells could be blocked to potentially prevent narcolepsy. They’re also eager to know whether other HLA-associated brain disorders, such as schizophrenia, are linked to autoimmunity.

People have long thought that the brain is somehow involved in the development of narcolepsy but, we’re learning this is wrong. Fortunately, narcolepsy seems to be a very simple disorder to use as a model. There is one HLA molecule involved, and there may be only one target, hypocretin. It will allow us to learn more about human autoimmune diseases. Mignot and Mellins are inventors on a patent to use the hypocretin epitope for narcolepsy diagnosis and to modify the HLA-A2009 epitope in influenza vaccines. Stanford owns the intellectual property rights for narcolepsy diagnosis, and GlaxoSmithKline owns the rights for vaccine improvements.

The Department of Psychiatry and Behavioral Sciences also supported the work.
Ludwig
continued from page 1

Cell Research and Medicine at Stanford. This gift is a testament to the growing confidence in the work of our colleagues at other Ludwig Centers and is doing and will provide essential support as they pioneer new treatments around the world.

The gift will complement Stanford’s Cancer Initiative, a $250 million effort to advance research and improve patient care. “This gift is consistent with the idea that virtual all cancers express CD47, known as CD47. They would later discover that this protein works particularly well when used in combination with other known anti-cancer agents, such as rituximab (a lymphoma drug) and trastuzumab (a breast cancer drug), effectively reducing or eliminating tumor growth entirely in a mouse model.

The evolutionary selection pressure to truly transform cancer research and treatment.” Weissman said. “Together for this exceptional gift, which will provide momentum for research participants, families, maintain jobs and lead normal lives. We need to do the pivotal trials to extend and expand the original studies.”

The study was funded by the Ellison Foundation, the National Institutes of Health, and the American Cancer Society.

Ludwig Cancer Research Fund has funded the work of some 10 to 15 laboratories at Stanford and has helped support Stanford’s collaboration with the University of Oxford. Researchers at both universities will be conducting CD47 trials in patients with leukemia and solid tumors.

Testosterone
continued from page 1

In the study, women had a generally stronger antibody response to the vaccine than men. But the average response among women to the vaccine, the analysis showed, was not significantly different than that of men.

The researchers analyzed test scores from 64 men and women, including those with low testosterone levels, who were given the influenza vaccine. Researchers believe that men who are more testosterone-dependent are less likely to respond to vaccines than women.

High testosterone levels were associated with reduced post-vaccination antibody responses among all men, but women did not show a significant relationship between testosterone levels and antibody responses.

Analysis of samples from 53 women and 31 men showed that testosterone levels were more or less equivalent to that of women.

It has long been known that, in general, women’s immune systems are more resistant to bacterial, viral, fungal and parasitic infection than men are, and this new study confirmed that.

Women don’t respond as strongly to vaccines as men for a variety of reasons. Women have more healthy immune cells and better control of their immune system after vaccination. They also have higher levels of regulatory T cells, which help to dampen the immune response.

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Analysis of samples from 53 women and 31 men showed that testoste...
Researchers awarded $12.7 million for cancer immunotherapy trials

By Krista Conger

Researchers at the School of Medicine have received a $12.7 million grant from the California Institute for Regenerative Medicine to move toward phase-1 clinical trials of an anti-cancer antibody called anti-CD47.

This round of grants, presented during a meeting of the agency’s governing board, is aimed primarily at furthering the development of previously funded, and successfully completed, CIRM projects.

The Stanford team, headed by Irving Weissman, MD, professor of pathology and of developmental biology, received $20 million from the agency for the project in 2009 to develop an antibody to CD47, a molecule that appears to protect the cells from attack by the immune system.

Researchers call CD47 the “don’t eat me” signal to destroy the cancer stem cells.

I think this is the sharp end of the CIRM program.”

Researchers at the Stanford Cancer Institute for Stem Cell Biology and Regenerative Medicine and the Virginia & D.K. Ludwig Center for Cancer Research in Cancer Research. He is also a member of the Stanford Cancer Institute.

Stanford’s funding was a portion of the roughly $61 million awarded Dec. 12 as part of the state stem cell agency’s third round of disease team grants.

“The goal of the Disease Team Award is to help accelerate the development of new therapies,” said CIRM president Alan Trounson, PhD. “I think this is the sharp end of the CIRM program — we need to get therapies into clinical trials. The scientists are working together as teams to demonstrate the safety and efficacy of their products that have evolved from discoveries in the laboratory. What’s impressive about this series of awards is that five of the six successful applications are for the continuation of work we had previously funded. It’s a reflection of the importance of continuity of funding, enabling scientists to keep their teams together and move their work forward as quickly as possible.”

With this award, Stanford has received about $290 million from the stem cell agency.

CIRM was established in November 2004 with the passage of a statewide ballot measure that provided $3 billion in funding for stem cell research at California universities and research institutions.

Free ‘statistical learning’ online course starts Jan. 21

A nine-week online course that begins Jan. 21 will teach students how to construct computational systems that learn from collected data and predict outcomes, a foundation of artificial intelligence.

The course and textbook, which is also online, are free.

In medicine, these data analysis techniques are becoming increasingly important for everything from interpreting the human genome to medical-image interpretation. For example, these methods could be used to tailor drug treatments for patients based on their genetic profiles, or to create a machine that diagnoses cancer by reading mammogram images.

To register for the course, visit https://class.stanford.edu/courses/HumanitiesScience/StatLearning/Winter2014/about. Please give blood

Blood type needed: O+, O-, A- and B+

To request an appointment, call 723-7831 or you can make an appointment online.

STANFORD BLOOD CENTER

3373 Elilade Ave, Palo Alto • 405 Burgess Drive, Menlo Park, 515 South Dr, Mountain View

http://bloodcenter.stanford.edu

Workshop on regulations for apps in health-care marketplace set for Jan. 28

A workshop on new U.S. Food and Drug Administration regulations for bringing mobile applications into the health-care marketplace will be held from 8:15 a.m. to 12:30 p.m. Jan. 28 in the Clark Center auditorium.

Designed for both novice and experienced developers, attendees will hear directly from the experts, including regulatory attorneys, regulatory affairs specialists, quality system experts, European law attorneys, experienced mobile health executives and FDA representatives.

This event is free to Stanford faculty, staff and students, and $100 for others. Register at http://biodesign.stanford.edu/bdn/networking/MMARRoadshow.jsp.

Medical school’s web design plans to be unveiled Jan. 22

Plans for the medical school’s new website design and web-publishing system will be unveiled at 10 a.m. Jan. 22 in room 120 of the Li Ka Shing Center for Learning and Knowledge.

Web authors and others interested in the website are invited to attend the Stanford Medicine Web Transformation Keynote. Space is limited to the first 120 people, so those who are interested are advised to come early or to watch the event live online at http://med.stanford.edu/web. Updates about the event will also be posted on that page.

Mark Trenchev, director of web services for the Office of Information Resources & Technology, said the event will launch the school’s next-generation web strategy and showcase a new publishing system that will “transform how we do the web at Stanford Medicine.”

He said the new design will empower school units to build sites targeted to their goals and end-users’ needs, while providing an integrated brand for the Stanford Medicine web experience.

Those who attend the meeting will be able preview the new publishing tools and see how the design looks and feels on computers and mobile devices.