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embryonic stem cells

For the first time in history, USC

researchers have derived authentic

enable scientists to create far more

effective animal models for the study

The research was published in the

"This is a major development in

stem cell research because we know

ed to humans than mice in many

direction of many labs around the

world will change because of the

availability of rat ES cells," said Qi-

Long Ying, assistant professor of cell

and neurobiology at the Keck School

of Medicine, researcher at the Eli

Regenerative Medicine and Stem

Cell Research, and the study's prin-

The finding brings scientists

much closer to creating "knockout"

genes-for biomedical research. By

observing what happens to animals

researchers can identify the function

of the gene and whether it is linked

tions for the creation of the disease model we want," Ying said. "The

availability of rat ES cells will greatly

facilitate the creation of rat models

for the study of different human dis-

eases, such as cancer, diabetes, high

Ying, a native of China, noted

occurred during 2008, the Chinese

Embryonic stem cells are derived

from a group of cells called the inner

embryo. ES cells provide researchers

with a valuable tool to address fun-

blood pressure, addiction and

that this breakthrough research

cell mass in a very early stage

damental biological questions,

because they enable scientists to

study how genes function, and to

develop animals with conditions that

See RAT, page 3

autoimmune diseases."

year of the rat.

"Without ES cells it is impossible to perform precise genetic modifica-

when specific genes are removed,

rats—animals that are genetically

modified to lack one or more

and Edythe Broad Center for

cipal investigator.

to a specific disease.

aspects of biology. The research

that rats are much more closely relat-

This breakthrough finding will

of a range of human diseases.

Dec. 26 issue of the journal Cell.

embryonic stem (ES) cells from rats.

USC researchers derive first rat

**By Meghan Lewit** 

**JANUARY 9, 2009** 

# Starnes to lead Keck Department of Surgery

## By Cheryl Bruyninckx

Dean Carmen A. Puliafito has named Vaughn A. Starnes chair of an expanded Department of Surgery at the Keck School of Medicine of USC, effective Dec. 1, 2008.

weekly

"I am delighted to appoint one of our own to this very important new role at the Keck School of Medicine," Dean Puliafito said. "Dr. Starnes is a stellar surgeon and academic leader who will play a pivotal role in building USC's new academic medical center."

Starnes holds the H. Russell Smith Foundation Chair for Cardiovascular Thoracic Research. He previously served as chair of the Keck School's Department of Cardiothoracic Surgery, which is being merged into the Department of Surgery along with the Department of Colorectal Surgery. He is the founding executive director of the USC Cardiovascular Thoracic Institute and chief of cardiothoracic surgery and director of the Heart Institute at Childrens Hospital Los Angeles.

As the chair of the Department of Surgery, Starnes' priorities include:

• Building on the foundation established by retired chair, Tom DeMeester, who served in the role since 1990, to create a top-flight academic surgical program.

• Recruitment of nationally recognized leaders in various surgical areas, including liver transplantation, breast



Vaugh A. Starnes is the new chair of the Department of Surgery at the Keck School.

surgery, thoracic surgery and colorectal surgery.

• Focus on the department's educational programs to be certain the residents and medical students are finishing the program with good exposure to advanced surgical techniques and satisfaction with their educational experience.

"We certainly have a very good foundation," said Starnes. "The model is going to be excellence in clinical care, along with excellence in surgical teaching." An internationally renowned surgeon, Starnes is acclaimed for his pioneering work in cardiothoracic surgery, heart and lung transplantation, and repair of congenital heart defects. He is also recognized for his expertise in heart surgery for children and newborns.

In 1990, Starnes performed the world's first lobar transplant using a lung segment from a living donor. Three years later, he performed the first live-donor, double-lobar lung transplant on a patient with cystic fibrosis. The operation involved taking lung tissue from each parent and transplanting it into their child.

"Dr. Starnes is a pioneer in the field of cardiothoracic surgery," noted Puliafito in an announcement to Keck School faculty and staff. "He has conducted more living donor lung transplants in adults and children than any other surgeon in the United States."

As the founding executive director of the USC Cardiovascular Thoracic Institute, Starnes has built an innovative, interdisciplinary powerhouse, comprised of clinicians and basic scientists who are exploring better and more innovative ways of treating heart disease. Under his leadership, USC surgeons have conducted more than 15,000 open heart surgeries to repair and replace valves or create coronary artery bypasses, and more than 10,000 surgeries for diseases of the lungs, See **STARNES**, page 3

USC scientist receives Presidential honor at White House

### By Sara Reeve

Li Zhang, assistant professor of physiology and biophysics in the Zilkha Neurogenetic Institute at the Keck School of Medicine, received the Presidential Early Career Award for Scientists and Engineers (PECASE) at a White House ceremony in December. The award is the nation's highest honor for scientists beginning their independent careers.

Zhang was recognized for his innovative research on the structure and function of neural circuitry in the auditory cortex. Zhang and 11 other National Institutes of Health (NIH)-supported researchers were selected by the White House Office of Science and Technology Policy to receive the prestigious award from President George W. Bush.

Zhang is the first NIH-supported scientist from USC selected for this award.

"This distinguished honor reflects upon the outstanding work of Dr. Zhang and all of our faculty at the Zilkha Neurogenetic Institute," said Keck School Dean Carmen A. Puliafito. "We look forward to Dr. Zhang's future contributions in this important area of science."

The Presidential Awards are intended to recognize and



Zhang (front row, second from left) and the eleven other NIH-supported researchers who received the Presidential Early Career Award for Scientists and Engineers at a White House ceremony in December.

nurture some of the finest scientists and engineers who, at the outset of their independent research careers, show exceptional potential for leadership at the frontiers of scientific knowledge.

# Keck researchers receive grant for new prostate cancer prognostic tool

### By Katie Neith

Researchers from the Keck School of Medicine have received a grant from the Southwest Oncology Group (SWOG) to move forward with an innovative clinical trial assessing a unique prostate cancer prognosis tool.

SWOG is one of the largest cancer clinical trials cooperative groups in the U.S. and is funded by research grants from the National Cancer Institute.

The \$200,000 grant will support the assessment of a new microfilter device used to capture circulating tumor cells (CTC), which are cells shed by tumors. Recent studies have shown that quantification of these cells can predict response to therapy and overall survival in advanced prostate cancer.

"We desperately and urgently need tools like this," said Amir Goldkorn, assistant professor of medicine and co-primary investigator of the study. "Right now, we are often giving a best guess as to how to treat patients."

Previous models of CTC collection have been limited by low yield, complex techniques and high costs. Goldkorn and his co-primary investigator Richard Cote, professor of pathology and urology, as well as co-investigators David Quinn, associate professor of medicine at the Keck School of Medicine, and Y.C. Tai, professor of electrical engineering at Caltech, have developed a cost-effective, easyto-use device that requires only a small peripheral blood sample to reliably trap and enrich CTCs.

The researchers will pass blood samples from a large national multi-center clinical trial through the microfilter to assess whether CTC counts of prostate cancer patients collected pre- and post-treatment accurately predict clinical outcome and response to therapy. They will also seek to predict response to therapy by assessing biomarkers expressed on the captured CTCs, as well as by evaluating the measurement of telomerase activity in the microfilter captured cells. Telomerase is an enzyme present in cancer.

"This has the potential to provide us with a very powerful tool," said Goldkorn. "It would allow us to prognosticate, or tell how a patient will do with their disease over time, and also predict who will respond to what treatment. In addition, it will allow us to monitor patients in real time as we treat them."

He added that, if successful, predicting clinical outcomes and response to therapy via the microfilter device would not be limited to just prostate cancer, but be applicable to the vast majority of cancer patients.



A REASON TO CELEBRATE—Irene West, a member of the Angel's West fundraising group, hands a check for \$30,000 to Keck School Dean Carmen A. Puliafito at the USC Norris Comprehensive Cancer Center holiday party held in December. Angel's West is a group of volunteers who have been donating funds for cancer research since July 1992, raising over \$1 million for USC Norris. The group raises money via member donations and the sale of entertainment books and tribute cards, gift certificates for See's Candy, supermarket scrip, sales of tickets to the Pageant of the Masters, and other activities.

# School of Dentistry study links drugs to jaw necrosis risk

#### By Beth Dunham

Even short-term use of common oral osteoporosis drugs may leave the jaw vulnerable to devastating necrosis, according to a new USC School of Dentistry study

appearing in the Jan. 1 *Journal of the American Dental Association (JADA)*.

"Oral Bisphosphonate Use and the Prevalence of Osteonecrosis of the Jaw: An Institutional Inquiry" is the first large institutional study in the U.S. to investigate the relationship between oral bisphosphonate use and jaw bone death, said principal investigator Parish Sedghizadeh, assistant professor of clinical dentistry with the School of Dentistry.

After controlling for referral bias and other patient health factors, nine of 208 School of Dentistry patients who take or have taken Fosamax for any length of

time were diagnosed with osteonecrosis of the jaw (ONJ). The study's results are in contrast to drug makers' prior assertions that bisphosphonate-related ONJ risk is only noticeable with intravenous use of the drugs, not oral usage, Sedghizadeh said.

"We've been told that the risk with oral bisphosphonates is negligible, but four percent is not negligible," he said.

Most doctors who have prescribed bisphosphonates have not told patients about any oral health risks associated with the use of the drugs, despite even short-term usage posing a risk due to the drug's tenacious 10-year half-life in bone tissue. Lydia Macwilliams of Los Angeles said no one told her about the risk posed by her three years of Fosamax usage until she became a patient of Sedghizadeh at the School of Dentistry.



Parish Sedghizadeh, assistant professor of clinical dentistry and principal investigator of the study.

"I was surprised," she said. "My doctor who prescribed the Fosamax didn't tell me about any possible problems with my teeth."

Macwilliams was especially at risk for complications because she was to have three teeth extracted. After her extractions, two of the three extraction sites had difficulty healing due to infection, Macwilliams said. Luckily, with treatment as well as the rigorous oral hygiene regimen that USC dentists developed especially for patients with a history of bisphosphonate usage, the remaining sites slowly but fully healed.

> "It took about a year to heal," she said, "but it's doing just fine now."

The infection is a biofilm bacterial process, meaning that the bacteria infecting the mouth and jaw tissues reside within a slimy matrix that protects the bacteria from

many conventional antibiotic treatments, and bisphosphonate use may make the infection more aggressive in adhering to the jaw, Sedghizadeh said. The danger is especially pronounced with procedures that directly expose the jaw bone, such as tooth extractions and other oral surgery.

Sedghizadeh hopes to have other researchers confirm his findings and thus encourage more doctors and dentists to talk with patients about the oral health risks associated with the widely used drugs. The results confirm the suspicions of many in the oral health field, he said.

"Here at the School of Dentistry, we're getting two or three new patients a week that have bisphosphonaterelated ONJ," he said, "and I know we're not the only ones seeing it."

# PECASE: USC scientist with leadership potential recognized

Continued from page 1

"The NIH is extraordinarily proud of these 12 PECASE winners who have, early in their research careers, shown exceptional potential for scientific leadership," Raynard S. Kington, acting NIH director, said. "Supporting new young scientists, particularly in these challenging economic times, is a priority for NIH. We look forward to continued success from these outstanding investigators as they push the frontiers of medical research."

Other NIH-supported PECASE award recipients came from universities across the country, including Case Western Reserve University; Cornell University; Harvard University; Robert Wood Johnson School of Medicine; the University of Maryland; the University of Texas, El Paso; the University of Vermont and the University of Washington. Two recipients came from the National Human Genome Institute at the NIH.

# **HS** week

## Phone: 323-442-2830 Fax: 323-442-2832 Email: hscwkly@usc.edu Web: uscnews.usc.edu/hscweekly/

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## Next Issue: January 16

Senior Vice President, University Relations: Martha Harris Contributors: Eva Blaauw, Cheryl Bruyninckx, Beth Dunham, Veronica Jauriqui, Meghan Lewit and Katie Neith

# Katkhouda named California chapter president of bariatric surgical society

#### By Meghan Lewit

Surgeon Namir Katkhouda has been named president of the California Chapter of the American Society of Metabolic & Bariatric Surgery (ASMBS).

Katkhouda, professor of surgery and director of the Keck School of Medicine's minimally invasive surgery program, is a leader in the development of bariatric, or weight loss, procedures. In 2002, he performed the first laparoscopic gastric bypass surgery at USC. Now, surgeons at the Keck School perform more than 300 obesity surgeries each year. "I am honored to have been elected by an executive committee of my esteemed colleagues in California to this post," Katkhouda said. "I believe that leadership is about service. In this new role I plan to foster scientific communication between the various bariatric groups in

California through

meetings and symposia."



Namir Katkhouda, professor of surgery at the Keck School of Medicine. include more private practitioners in the chapter, to push surgical innovation in California and to act as a patient advocate to the insurance companies.

The ASMBS is the largest society in the world dedicated exclusively to metabolic and bariatric surgery.

*sur-* The national organiza*dicine.* tion aims to advance the

science of bariatric surgery and super-

vises the designation of center of excel- tion

lence in bariatric surgery to hospitals and institutions.

The USC Bariatric Surgery Program at USC University Hospital is one of more than 300 centers of excellence in the U.S.

Katkhouda estimates that the surgeons in Southern California perform 10 percent of all the nation's bariatric surgeries.

"Bariatric surgery is one of the fastest growing procedures and California is pre-eminent in these kinds of surgeries," he said. "It is important to integrate and encourage more communication among practitioners."

# RAT: Development of rat stem cells is major advance in biomedical science

#### Continued from page 1

mimic important human diseases.

The first ES cell lines were established from mice in 1981 by Martin Evans of Cardiff University, U.K., who was last year awarded the Nobel Prize in Medicine or Physiology. Researchers have long been working on establishing rat ES cells, but faced technical hurdles because the conventional methods developed for the derivation of mouse cells did not work in rats.

Building on recent research into how ES cells are maintained, the USC researchers found that rat ES cells can be efficiently derived and grown in the presence of the "3i medium," which consists of molecules that inhibit three specific gene signaling components (GSK3, MEK and FGF receptor kinase). This approach insulates the stem cell from signals that would normally cause it to differentiate, or turn into specialized types of body cells. By blocking these signals, Ying and colleagues found that stem cells from rats, which have previously failed to propagate at all, could be grown indefinitely in the laboratory in the primitive embryonic state.

Katkhouda said he also hopes to

An accompanying study led by researchers at the University of Cambridge, U.K., reported similar findings, independently verifying that authentic ES cells can be established from rats.

"The development of rat embryonic stem cells, long sought by researchers around the world, is a major advance in biomedical science," said Martin Pera, director of the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research. "These new stem cell lines will make a huge contribution to basic and applied research and drug development, by providing a technology platform for facile genetic manipulation of a mammalian species that is widely used in academic and industrial labs studying physiology, pathology and pharmacology." Until now, authentic

Until now, authentic ES cells have never been established from humans or animals other than mice. This new key understanding into how ES cells are

maintained in culture may eventually enable scientists to establish real ES cell lines from a number of other mammals, which could have significant implications for organ transplantations and the development of drug therapies, Ying said. Researchers at USC are currently working on generating the first gene



Qi-Long Ying, assistant professor of cell and neurobiology and the study's principal investigator.

knockout rat through ES cell-based technologies.

"If our work is feasible it is likely that many labs will follow up to generate different types of gene knockout rat models," he said. "This will have a major impact on the future of biomedical research."

# STARNES: Top priority to make USC the 'place to be' for surgery on the West Coast

#### Continued from page 1

esophagus and chest wall. Starnes and his surgical team also performed Southern California's first robotic heart operation in 2001 as part of a clinical trial evaluating the use of a remote surgical system.

For his outstanding work, Starnes has received numerous prestigious awards. In 2008, he was awarded the Presidential Medallion from USC for his significant contributions to cardiothoracic medicine and transplantation, his distinguished career as a healer and educator, and his dedication to the advancement of human health and well-being. Starnes is also consistently listed among the "Best Doctors in America" and "America's Top Doctors."

In addition to his clinical work, Starnes is a distin-

# In Case of An Emergency...

#### Visit the USC Web:

http://emergency.usc.edu

This page will be activated in case of an emergency. Backup Web servers on the East Coast will function if the USC servers are incapacitated.

# Call the Emergency Information Phone: 213-740-9233

The emergency telephone system can handle 1,400 simultaneous calls. It also has a back up system on the East Coast.

guished researcher. He has an ongoing interest in many areas of research, including congenital heart disease, cadaveric and live-donor organ transplantation, coronary bypass grafting, and repair and replacement of heart valves. He is also involved in bench research, helping develop gene therapy techniques to address

problems that occur after balloon angioplasty procedures.

Starnes is currently investigating the use of gene therapy to prevent scarring following heart surgery. He is also involved in a clinical trial using robotic surgery technology for cardiothoracic surgery. "My priority is really to create a top-flight academic surgical program," said Starnes. "I think patients are going to come to USC because they view it as the best place to be for surgery on the West Coast."

# January is National Blood Donor Month

Individuals who want to donate blood will have the opportunity at two upcoming blood drives on the Health Sciences Campus. All donated blood will benefit patients at USC University and USC Norris Cancer hospitals.

1/9—USC Norris Cancer Hospital (near valet parking); 9 a.m. - 3:30 p.m. 1/20—Hoffman Medical Researcg Building lobby; 10 a.m. - 4 p.m.

The USC Blood Donor Center is also open Monday through Thursday from 8 a.m. to 6 p.m. for those with schedule conflicts.

Blood is traditionally in short supply during the winter months due to the holidays, travel schedules, bad weather and illness. Every day in the United States, approximately 39,000 units of blood are required in hospitals and emergency facilities for patients with cancer and other diseases, for organ transplant recipients, and to help save the lives of accident victims.

For more information, call the USC Blood Donor Center at (323) 442-5433 (LIFE).

# **Calendar of Events**

## The HSC Calendar is online at www.usc.edu/hsccalendar

## Monday, Jan. 12

NOON. Visions and Voices the USC Arts & Humanities Initiative. "The Spirit Catches You and You Fall Down," Anne Fadiman. KAM Mayer Auditorium. Info: visionsandvoices@usc.edu

## Tuesday, Jan. 13

NOON. Cancer Ctr. Grand Rounds. "Cancer Survivorship: The Pediatric Perspective," David Freyer, USC. NOR 7409. Info: (323) 865-0801

## Wednesday, Jan. 14

NOON. "Synaptic Integration and Plasticity in Hippocampal Pyramidal Neurons," Nelson Spruston, Northwestern Univ. ZNI 112. Info: (323) 442-3219

## Thursday, Jan. 15

NOON. "Medicine for the Soul," Rishi Manchanda, St. John's Well Child and Family Center. MCH 149. Info: (213) 740-6110

### Friday, Jan. 16

**8:30** A.M. "The Road to Resolution: Role of IGF Pathways in Lung Injury and Repair," L.M. Schnapp, Univ. of Washington. GNH 11-321. Info: (323) 226-7923

**9** A.M. USC Childhood Obesity Research Ctr. Seminar. "Genetics and Obesity: An Overview and Results from the Children's Health Study," Fredrick Schumacher, USC. CSC 250. Info: (323) 442-2637 **11** A.M. Hematology Grand Rounds. "ASH Updates on Multiple Myeloma," Sikander Ailawadhi, USC. IPT C2J103. Info: (323) 865-3950

#### Wednesday, Jan. 21

7 P.M. "This land Is OUR Land...Greening, Architecture, Ethics and the Environment," Ian Ritchie. UPC Bovard Auditorium. Info: visionsandvoices@usc.edu

### Friday, Jan. 23

NOON. Hematology Grand Rounds. "ASH Updates on Chronic Lymphocytic Leukemia and Lymphomas," Ann Mohrbacher, USC. IPT C2J103. Info: (323) 865-3950

## Tuesday, Jan. 27

NOON. Cancer Ctr. Grand Rounds. "Chemical Engineering of Protein Splicing for Protein Function and Structure Studies and For Targeted Therapies," Julio Camarero, USC. NOR 7409. Info: (323) 865-0801

## Wednesday, Jan. 28

Noon. "The Role of Regulated Protein Synthesis in Visual Circuit Development," Hollis Cline, Watson School of Biological Sciences. ZNI 112. Info: (323) 442-3219

**Notice: Deadline for calendar submission is 4 p.m. Monday** to be considered for that week's issue—although three weeks advance notice of events is recommended. Please note that timely submission does not guarantee an item will be printed. Send calendar items to HSC Weekly, KAM 400 or fax to (323) 442-2832, or e-mail to eblaauw@usc.edu. Entries must include day, date, time, title of talk, first and last name of speaker, affiliation of speaker, location, and a phone number for information.

# **HSC NEWSMAKERS**

On Jan. 6, the *Los Angeles Downtown News* ran an *HSC Weekly* article on a study led by cancer researcher **Michael Lieber** which explains how certain key mutations occur in human lymphomas.

On Jan. 1, ABC News quoted OB/GYN **Donna Shoupe** about the osteoporosis drug Fosamax.

A Dec. 29 *Kansas City Star* article quoted ophthalmologist **Mark Humayun** about the artificial retina project.

A Dec. 28 *Los Angeles Times* article noted that USC Norris urologist **John P. Stein** passed away in 2008.

Two Dec. 24 *Washington Post* articles quoted stem cell researcher **Qi-Long Ying** and reported that the first embryonic stem (ES) cells from rats have been derived by researchers at the Keck School of Medicine. *U.S. News & World Report* and WAVE3-TV also ran stories on the research. A Dec. 24 U.S. News & World Report article quoted neurology researcher Michael Jakowec about a study which found that people with a disorder that causes them to kick or cry out during deep sleep are more likely to develop dementia or Parkinson's disease.

Complete listing at: www.usc.edu/uscnews/usc\_in\_the\_news/

A Dec. 22 *Los Angeles Times* article quoted USC Norris cancer researcher **Heinz-Josef Lenz** about the effectiveness of colonoscopy.

A Dec. 18 *Seattle Times* article noted that the Eli and Edythe Broad Foundation gave \$30 million to the University of Southern California to boost stem cell research. The donation was also noted in the *San Jose Mercury News*, the *Los Angeles Business Journa*l and on Yahoo News and KCBS-FM.

On Dec. 12, MedCenterToday online posted a *USC News* article on **Vaughn A. Starnes** being named chair of an expanded Department of Surgery at the Keck School.



**NEW YEAR, NEW LOOK**—Visitors may have noticed a new look to the Keck School of Medicine of USC Web site at www.usc.edu/keck. The home page for the school has been revamped to include a new rotating slideshow, as well as quick links to the school's education, research and patient care portals. The new home page went live in late December.

## Professor receives honor from Queen Elizabeth II

David Warburton, director of the Developmental Biology and

Regenerative Medicine Program and vice chair of the Department of Surgery at Childrens Hospital Los Angeles, will be named an Officer in the Most Excellent Order of the British Empire (OBE)

from Queen Elizabeth II at David Warburton ceremonies in London in the spring. Warburton also is professor of pediatrics and surgery at the Keck School of Medicine, and professor of craniofacial biology at the School of Dentistry.

Warburton was listed on the Foreign Office and Overseas List for service to

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scientific collaboration between the United States and the United Kingdom.

"This is indeed a great honor," said Warburton. "This means I owe a great debt of gratitude to everyone in the collective Childrens Hospital Los Angeles and USC Family, and the honor is really for them."

Warburton leads a team of 60 researchers in developmental biol-

ogy, regenerative medicine and surgery at The Saban Research Institute of Childrens Hospital Los Angeles. The team studies organ development and regeneration, as well as different tissue engineering solutions for lung, kidney, bladder, liver and diabetes.

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