

## USC/Norris receives \$5 million gift for Breast Center

Even before cancer touched their lives, Henrietta C. Lee and her husband Harold planned to play a significant role in the fight against the disease by leaving the majority of their estate to fund medical research.

But after the illness claimed Harold's life and ovarian cancer struck the Lees' niece Patricia R. Jones, Henrietta Lee grew more eager to support current research to help cure the disease.

About that time, she received a letter from the USC/Norris and Art Ulene, chair of the Norris Development Board and former NBC "Today Show" medical consultant, that pointed to the desperate need for private donors to fund promising research that would otherwise languish.

Lee took the message to heart and recently entered into discussions with John Baker, director of major gifts for the USC/Norris, about what she could do to help.

Last week, Lee personally delivered the first installment of a \$5 million gift to expand and improve the Norris' Breast Center into a state-of-the-art research and treatment facility and recruit top physicians and researchers to lead it.

Named for Lee and her husband, the 5,000 square foot Harold E. and Henrietta C. Lee Breast Center will be located on the first floor of the USC/



Henrietta Lee is giving \$5 million to expand the USC/Norris Breast Center. Mel Silverstein, right, will serve as medical director for the Center; Michael Press, left, will hold an endowed chair in cancer research.

Norris Hospital and is expected to open sometime in the fall.

Lee said that aiding the Cancer Center fulfills a dream she shared with her husband: "I feel honored to be able to do this because I knew that the USC/Norris has been doing a wonderful job fighting cancer and I wanted to help."

Ulene praised Lee's generosity and vision, saying that "she has come

through with an extraordinary gift that will fund both research and clinical care and make a huge difference in the lives of women for years to come. It is private donations like these that allow us to take the first steps with innovative projects that, in my opinion, will ultimately lead to the cure for cancer."

Ulene also said he was struck by the unassuming manner in which Lee

made possible such a major advance for the Norris.

"We tried to impress upon her the enormous importance of this gift but she's such a modest person that she refused to take personal credit. We were all just amazed by the generosity and humility of this woman. As far as she is concerned, this was simply the right thing to do. She told us she was grate-

ful she could do it," he said.

Cancer Center Director Peter Jones, director of the Cancer Center, said the gift, among other benefits, has enabled the USC/Norris to recruit Mel Silverstein, an internationally respected surgeon and specialist in research and clinical treatment of breast cancer.

Silverstein, who developed the acclaimed Van Nuys Breast Center and wrote a definitive book on breast cancer, has agreed to head the new center. He will serve as medical director of the Breast Center and co-leader of the breast cancer research program, Jones said.

Silverstein will hold one of two endowed chairs in cancer research. The other will be filled by Michael Press, professor of pathology and medicine. Press is the USC/Norris' leading basic scientist in the study of the molecular and genetic causes of breast and ovarian cancer, Jones said.

Baker called the \$5 million gift "one of the most important ever given to the Norris because of the number of people it will help. It will help create one of the premier breast centers in the nation and help us provide the most modern equipment for the diagnosis and treatment of breast cancer," he said.

"It's a landmark gift for us. It's really incredible," he said.

—Jon Nalick

## Rare honor awarded to researcher—twice

### Neurobiologist Jean Shih recognized for outstanding research

Success tastes just as sweet the second time around for USC's Jean Chen Shih, the Boyd and Elsie Welin Professor of Molecular Pharmacology and Toxicology at the School of Pharmacy with a joint appointment in Cell and Neurobiology at the School of Medicine.

Recently, Shih learned that she will receive a second MERIT Award from the National Institutes of Health, a competitive honor bestowed on fewer than 1 percent of researchers who apply for federal funding. Most researchers are pleased to get just one.

"Dr. Shih's work exemplifies the excellence in research conducted by faculty in the School of Pharmacy," said Timothy M. Chan, Dean of the USC School of Pharmacy. "Her accomplishment is unparalleled. We are very proud of her."

"It's wonderful to get this kind of recognition for our work," said Shih, who has done ground-breaking research on the biological roots of violence and, more generally, on how brain chemicals affect behavior.

"Jean is an outstanding neuroscientist," said Cheryl Craft, professor and chair of cell and neurobiology in the School of Medicine. Being selected for two of these special grants "is an amazing feat," Craft said.

In 1988, Shih was among 215 scientists selected from thousands of NIH grant applicants to receive a MERIT Award. The MERITs, or Method to Extend Research in Time, doubles the period of research funding from 5 years to ten.

Investigators don't apply for the awards. Instead, NIH division staff nominate stand-out R01 grant appli-

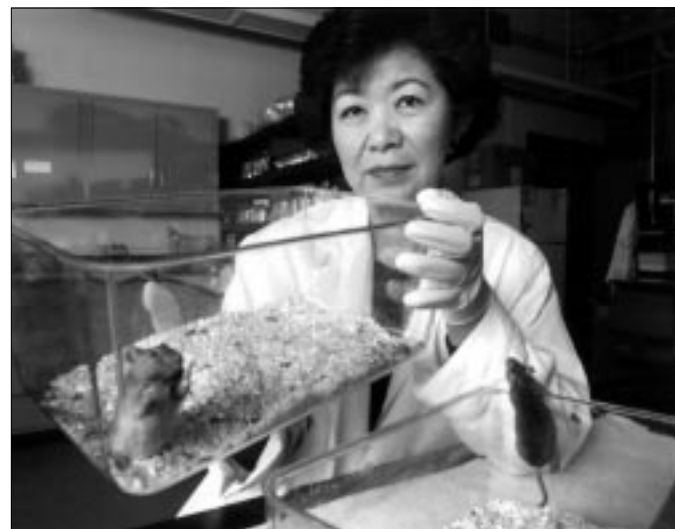
cants for the special honor.

Founded in 1986, the goal of the MERIT program is to allow innovative and productive scientists to spend less time applying for grant money and more time doing research.

Since 1991, the number of MERIT awards has dropped sharply. Last year, only 50 researchers were chosen from the thousands applying for R01 grants, according to data from the NIH Web site. Although he has no record of how many researchers have received two MERIT awards, NIH program analyst Bob Moore says it's exceedingly rare.

That makes Shih's news of a second award—this one for \$5.4 million over the next decade— even more significant.

Shih has made "a series of outstanding contributions.... Her approach has always been simple, direct and highly



Jean Shih, has received a second MERIT Award from the National Institutes of Health, a competitive honor bestowed on fewer than 1 percent of researchers who apply for federal funding.

effective," wrote the NIH grant review committee in their evaluation of her grant application.

Shih, who joined the USC faculty in 1974, has a long list of scientific accomplishments. She elucidated the key

role of an enzyme, monoamine oxidase (MAO), in the regulation of four major neurotransmitters that influence behavior. Her team isolated and cloned the genes that encode for the

See **SHIH**, Page 4

# CHLA throws its doors wide open on the World Wide Web

In an effort to bolster its accessibility to the public, Childrens Hospital Los Angeles launched its first official web site on Aug. 3, featuring almost 500 pages of information about the hospital's services, specialty centers and physicians.

Publications Manager Tim Bradley said the new site is designed primarily for patients and their families, making it easy for them to obtain care.

"It's geared to the parent with a kid having symptoms so they can locate physicians. Literally, millions of people can now connect to us almost instantaneously," he said.

He said that, in addition, the site can be used to facilitate fundraising efforts, help publicize the hospital's researchers and let outside researchers know which physicians at CHLA are serving as principal investigators for clinical trials.

Bradley said the next phase of web site development will offer more interactivity, including opportunities for visitors to learn about specific diagnoses and treatments and take virtual tours of the hospital.

Barclay E. Smith, vice president of business development and managed care, said the site replaces an unofficial web page that offered basic information about the hospital but little else.

The new version greatly expands the amount of information available and provides a new way to provide exposure for the hospital.

"We're the number one pediatric hospital in the West and not everyone knows that. This provides another way to get the word out," he said.

The new site, located at [www.chla.org](http://www.chla.org) will be monitored to see how often visitors access it and, eventually, to see how helpful the site is at steering visitors to the department or physician they are seeking.

"We want to make sure that if we get a request for information about pediatric cancer, it gets to the right place. We intend to track and follow up on the kinds of responses we give back to the users of the web site. Our feeling is: why spend all the money if it really isn't a tool?" Smith said.

—Jon Nalick

## When faith demands 'bloodless' surgery, USC delivers

A decade ago, Jehovah's Witnesses were frequently forced to choose between their faith — which prohibits any kind of blood transfusion — and their health. Many doctors refused to perform complex surgical procedures without the option of a blood transfusion.

"It was very adversarial," recalls Randy Henderson, coordinator of the USC Transfusion-Free Medicine and Surgery Program at USC University Hospital and USC/Norris Comprehensive Cancer Center and Hospital. "Doctors were not always open-minded enough to sit down and discuss alternative procedures."

Henderson is at the forefront of an effort to change that attitude — a cutting-edge USC program that studies and implements surgical techniques that minimize blood loss and reduce the need for transfusion.

Up to 4 million patients receive blood transfusions each year in the U.S., according to the American Association of Blood Banks. But thanks to advances in surgical and medical techniques and technology, more and more patients who request transfusion-free surgery are being accommodated at USC, Henderson said. In addition to those whose religious beliefs prohibit transfusions, he said, there are increasing numbers of patients who want to avoid even minimal risks associated with blood transfusions.

At USC, more than 100 physicians in a wide variety of disciplines — from neurosurgery and orthopaedics to otolaryngology and oncology — have signed on with the Transfusion-Free Medicine and Surgery Program. That means they will, at a patient's request, use techniques to minimize blood loss, including:

- using lasers rather than scalpels;
- stimulating bone marrow to produce red blood cells in advance of a procedure;
- enhancing circulation of the patient's own blood during surgery through volume expanders or intravenous fluids;
- using cell savers — technology that recycles a patient's own blood during surgery — to collect, recirculate and readminister the patient's own blood;

- speeding clotting during surgery with an argon beam coagulator;
- using an anesthesia that lowers blood pressure during surgery, minimizing bleeding.

"I think they have really raised the bar," Henderson said of the USC physicians.

When patients come to the Transfusion-Free Medicine and Surgery Program, said Henderson, they receive counseling in the various methods used to minimize blood loss and then consent to the specific procedures with which they and their physicians feel comfortable. They can refuse the alternatives they dislike.

To assure that a patient's wishes are respected, upon admission several security measures are put into place to help identify them as participants in the Transfusion-Free Program, including yellow-colored identification bands and flags on all charts and computerized patient lists.

In the past two years, more than 300 patients have participated in the Transfusion-Free Medicine and Surgery Program. Transfusion-free procedures have included liver resections, hip revision and replacement surgeries, cancer biopsies

and vascular procedures.

Technological advances have helped the Transfusion-Free Program become a more realistic possibility for many patients in the past few years. New drugs that lower blood pressure and prevent bleeding have only been available in the last four or five years. In addition, fairly new monitoring technology allows anesthesiologists to fine-tune blood pressure and oxygen levels.

Because of their role as researchers at the USC School of Medicine, many of the participating physicians are trying new procedures to minimize blood loss that are not yet available in most hospitals. For example, when Robbin Cohen, M.D., assistant professor of cardiothoracic surgery, was brought in on the case of Marie Jackson, there weren't many options: the 59-year-old Pasadena resident needed open heart surgery to replace a faulty mitral valve. But as a Jehovah's Witness, she had religious objections to receiving donor blood.

Since 30 to 40 percent of patients undergoing open heart surgery need transfusions, the best alternative Cohen could offer was a relatively new

procedure called port access surgery — where the valve could be replaced through a small four inch incision, or "port," on the side of the chest between the ribs. No sawing through the breastbone, no spreading the rib cage to reach the heart, and, most importantly for Jackson, no blood transfusion.

"It's great peace of mind," Henderson explained. "There is security in knowing that your wishes will be respected."

—Phil Davis and Monika Guttman

**Editor's Note: HSC Weekly is now on its summer publishing schedule with new issues appearing about every two weeks.**

### HSC Weekly

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## Ophthalmologist receives international honor

In the Olympics of the ophthalmology world, Ronald E. Smith, USC professor and chair of ophthalmology, has won gold.

As part of the 23<sup>rd</sup> International Congress of Ophthalmology, Smith was awarded a gold medal by the International Uveitis Study Group for his life's work.

He also delivered a special lecture at the Amsterdam meeting.

The committee which awarded the medal to Smith chose him in light of his significant contributions to the advancement of knowledge in the field of uveitis and appreciable contributions to the field of ophthalmology in general.

In a nominating letter, Narsing Rao, USC professor of ophthalmology, praised Smith's high standards in basic and clinical research, education, community service and leadership.



Ronald Smith

"By virtue of his numerous contributions to our understanding of ocular inflammation from epidemiologic studies, to laboratory research of animal models of ocular inflammation, to his clinical research of numerous uveitic syndromes, [Smith] has become a clinician and vision scientist of national and international reputation," Rao wrote.

"Dr. Smith is indeed one of the prominent clinician-scientists in the field of uveitis today," Rao added.

Smith has been a full-time faculty member at USC School of Medicine and the Doheny Eye Institute since 1975.

# Finasteride does not prevent prostate cancer, USC study finds

## Study suggests the drug could leave certain men at higher risk

A new study by USC/Norris Cancer Center scientists raises serious questions about the potential use of the drug finasteride to prevent prostate cancer.

Scientists had theorized that finasteride, sold under the brand name Proscar and commonly used to treat benign prostate disease, might offer men a way to cut their risk of developing prostate cancer.

Yet, "it appears that finasteride may not be effective as a chemopreventive agent against prostate cancer, at least in men with high PSA levels," said Ronald K. Ross, professor of preventive medicine and deputy director of the USC/Norris Cancer Center.

"There may even be a subgroup of patients in whom the drug actually could be harmful," said Richard Cote, associate professor of pathology and urology. Ross, Cote, and Eila C. Skinner, associate professor of urology, led the study, which appears in the August issue of the *British Journal of Cancer*.

Prostate cancer is the most frequently diagnosed cancer in the United States, and proves fatal for some 40,000 men each year. At present, there's no proven way to prevent the disease.

USC/Norris researchers have long led research on the role of the male hormones (androgens) in spurring prostate cancer growth. Ross and his colleagues first proposed that lowering levels of the androgen most active in the prostate, called dihydrotestosterone (DHT), could possibly prevent prostate cancer.

Ross' team was also the first to suggest that finasteride, which lowers the levels of DHT by blocking the enzyme that converts testosterone into DHT, might prevent the formation of pros-

tate cancer.

The National Cancer Institute (NCI) is in the midst of a large national clinical trial to determine if finasteride can reduce the incidence of prostate cancer. The seven-year NCI study has enrolled more than 18,000 healthy men with normal PSA levels.

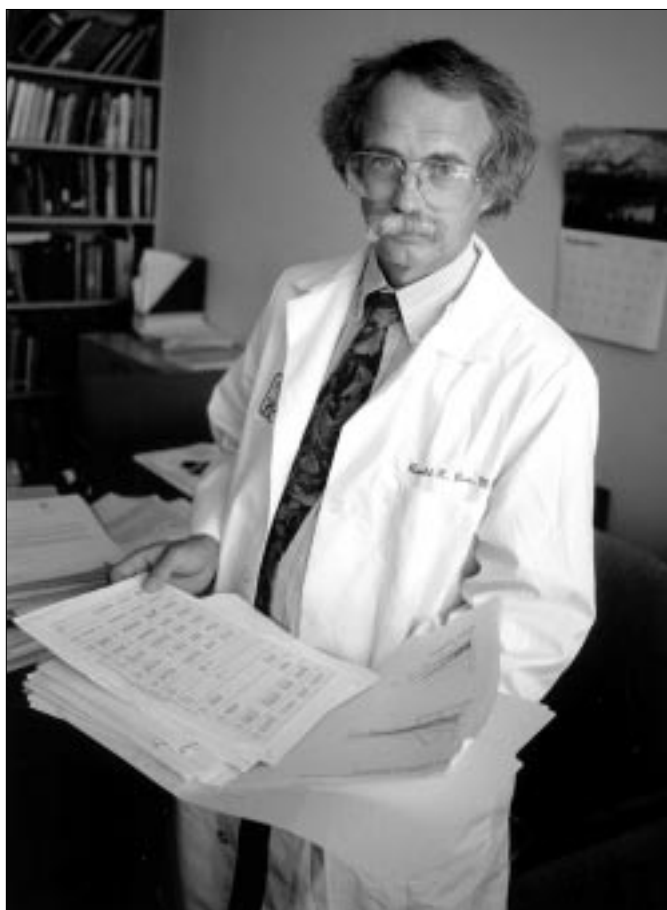
Right now, finasteride, manufactured by Merck & Co., is used most commonly to shrink the enlarged prostate glands of men with benign prostate hyperplasia and thereby improve symptoms. A lower dose of finasteride was approved by the FDA last year to treat cosmetic, incipient hair loss and is marketed under the brand name Propecia.

Although small, the new USC/Norris study seems especially significant in light of this ongoing trial, researchers say. "Ours are the first data to address the question of whether finasteride prevents disease. The results are not reassuring," Ross said.

In contrast to the NCI study (which is focusing on healthy men), the USC team studied 52 men with elevated blood levels of PSA (prostate specific antigen) whose biopsies showed no signs of prostate cancer. PSA is a protein produced only by prostate cells that doctors use as a broad, though fallible, screen for prostate cancer. Because all of the men in this study had elevated PSA levels, they were considered to have a higher risk of developing prostate cancer than men with normal PSA levels.

Half of the men were treated with finasteride for one year, while the other half received no treatment.

At the end of the study, a second biopsy revealed that eight of the 27 men who took the drug had developed tu-



'Ours are the first data to address the question of whether finasteride prevents disease. The results are not reassuring.'  
—Ronald K. Ross, professor of preventive medicine and deputy director of the USC/Norris Cancer Center

mors, compared to only one of the 25 men in the observation-only group.

To evaluate the drug's ability to block tumor development, Cote, Ross and Skinner tracked key intermediate markers of disease, a novel approach to testing new chemopreventive agents. They measured the participants' blood levels of testosterone, PSA and dihydrotestosterone; they also compared tissue samples from the biopsies at the start of the study to those at the end.

While men in the control group showed no changes in blood levels of PSA, testosterone or dihydro-testoster-

one, the treated men's PSA levels dropped by 48 percent and dihydrotestosterone levels fell by 67 percent. However, men in the treatment group saw their testosterone levels rise by 21 percent during the study.

The team also looked at tissue samples for a marker of benign disease — called hyperplastic epithelial tissue — and two markers associated with increased risk of prostate cancer — the presence of precancerous lesions known as PIN (prostate intraepithelial neoplasia) and the rate of cell proliferation in the prostate gland. They found that, as expected, finasteride re-

duced the proportion of the hyperplastic epithelial tissue. But, the drug had no effect on PIN or proliferation, which are more strongly linked to the development of cancer.

The results suggest that though finasteride lowers DHT levels, the net effect of hormones acting on the prostate may be unchanged by the drug, according to Ross. That may be because of rising testosterone levels in the men taking finasteride. Although not as potent as DHT, testosterone can also spur prostate cell growth. "The biology is not as straightforward as many people have assumed," Ross concludes.

Notably, of the eight men who had precancerous PIN lesions at the start of the study and treated with finasteride, six developed cancer after one year. In comparison, in the no-treatment group, none of the five men with precancerous PIN lesions got cancer. This finding, though in a small sub-group of the men, was statistically significant, leading researchers to write, "finasteride is unlikely to be useful and may even be harmful in men with PIN."

"If finasteride were to have had an anti-cancer effect, it is likely that it would have showed up in these patients," Ross said. The USC team holds off, however, on predicting the results of the national trial.

"It is possible that the drug could have a beneficial effect in preventing prostate cancer in some men, though the results of this study suggest that this is unlikely," he said.

Richard J. Cote, Eila C. Skinner, Carol E. Salem, Susan J. Mertes, Frank Z. Stanczyk, Brian E. Henderson, Malcolm C. Pike, and Ronald K. Ross. "The effect of finasteride on the prostate gland in men with elevated serum prostate specific antigen (PSA) levels." *British Journal of Cancer*, vol. 78, No. 3, August 1998.

—Eva Emerson

## CHLA and China formalize pediatric medicine collaboration

What started in 1986 as an informal exchange among pediatricians in Los Angeles and Beijing has become the first agreement to advance pediatric medicine struck between the People's Liberation Army's (PLA) General Hospital and Post Graduate Medical School in Beijing, and U.S. medical facilities.

The U.S. entities are Childrens Hospital Los Angeles (CHLA), University Childrens Medical Group (UCMG), Los Angeles, and Kapi'olani Health Research Institute in Honolulu.

These organizations have come together to begin a dialogue and work with Chinese physicians to improve pediatric care in some 200 PLA hospitals while enriching American pediatricians' understanding of medical practice in China. The program will also design and develop a collaborative pediatric research project and focus on ways to provide cost-effective, quality health care in both China and the U.S.

"This agreement greatly expands and formalizes a process that has been under way for several years between China and CHLA," said Walter W. Noce, Jr., president and CEO of CHLA.

Stuart Siegel, professor of pediatrics, has visited the PLA Hospital four times

since 1986 and CHLA physicians have been discussing medical cases and protocols with Chinese pediatricians for the past three years via the Internet.

In December 1997, a joint research and training program was inaugurated between the PLA General Hospital, CHLA, UCMG and Kapi'olani Health Systems to establish fellowships for Chinese physicians to receive training in pediatric hematology/oncology. To date four physicians have participated in the training program.

The overall agreement, signed June 16 in Beijing, aims at developing cooperative efforts and the exchange of information related to clinical medicine, research, nursing and information systems.

Regarding research, Siegel explains that each year in the U.S. there are 400-500 new cases of neuroblastoma, or childhood cancer of the peripheral nervous system, while in China there are more than 3,000 new cases annually. "The sheer size of the Chinese population opens up increased opportunities to study such diseases as neuroblastoma as we jointly search for a cure."

—Mary Ellen Stumpfl

## Etcetera

**Peter Conti**, professor of radiology and director of USC PET Imaging Science Center, has been elected to the board of directors of the Society of Nuclear Medicine for a three-year term.

Conti will also serve as chair of the scientific program of the Society's annual meeting.

Conti is an expert in brain tumor imaging, magnetic resonance imaging and spectroscopy and the development of PET-specific radiopharmaceuticals for the imaging of cancer and other diseases.

# Foundation awards \$350,000 to young USC researchers

Noting the caliber of research taking place at USC, the Donald E. and Delia B. Baxter Foundation recently announced they would continue to support young scientists at the School of Medicine with a gift of \$350,000.

"Since the 1960s, the Baxter Foundation has helped to maintain the research enterprise at the School of Medicine," said Stephen J. Ryan, dean of the medical school. "We deeply appreciate the substantial contributions the Foundation has made to support young researchers and educate medical students."

This year's grantees include Baruch Frenkel, assistant professor of orthopedics and of biochemistry and molecular biology, and Peter C. Brooks, assistant professor of biochemistry and molecular biology. Each will receive \$150,000 for laboratory studies.

In addition, \$50,000 will go to sustain the Baxter Foundation Research Fellowship program for medical students. In 1997, the program funded 28 student research projects.

Delia Baxter established the Baxter Foundation in 1959 in honor of her husband, Donald Baxter, who died in 1935. Donald Baxter, a physician and engineer, pioneered the commercial preparation of intravenous solutions, paving the way for widespread use of intravenous therapy. The foundation awards grants for research to leading postgraduate private institutions on the west coast.

The award will fund one of Frenkel's main research projects — figuring out

why long-term use of glucocorticoids, known as steroids, brings on bone-density loss and, in the worst cases, severe osteoporosis.

Doctors prescribe steroids for a wide range of chronic conditions, including arthritis, lupus and asthma. Many patients take the immune-suppressing drugs for years.

*This year's grantees include Baruch Frenkel, assistant professor of orthopedics and of biochemistry and molecular biology, and Peter C. Brooks, assistant professor of biochemistry and molecular biology. Each will receive \$150,000 for laboratory studies.*

"My interest in this started from the clinical problems seen from the side effects of glucocorticoids," said Frenkel, who believes that steroids are over-prescribed. "In chronic users, there may be 10 to 20 percent bone loss in the first year on the drug. Many patients will eventually develop bone fractures."

For susceptible people taking steroids "there's very little you can do about losing bone, except not take the drugs. Yet, the pain of arthritis and complications of other diseases may be so bad, many patients will not stop. That makes finding the solution to drug-induced bone loss even more important," he said.

Before he got into bones, Frenkel was all about teeth. He practiced dentistry while embarking on his doctoral research project.

"The teeth and bones develop in many of the same ways," said Frenkel, who left his native Israel to conduct re-

search in the United States. Since 1991, he has studied the molecular mechanisms that govern gene expression in bone cells. Frenkel has been at USC's Institute for Genetic Medicine since last fall.

In his study of drug-induced bone loss, Frenkel hopes to study how steroids affect osteoblasts, bone cells that continually replenish the skeleton. "Stress, a diet low in calcium might speed up the break down of bone. But under normal conditions, osteoblasts pick up the slack and restore the lost bone mass," he said. Glucocorticoids, it turns out, target osteoblasts (among other cells), dampening the bone cell's activity.

Steroids can block synthesis of collagen, a critical early step in generating the three-dimensional structure of new bone. Frenkel will explore other important genes also directly and indirectly repressed by the steroid.

"My goal is to understand at a molecular level how steroids inhibit the osteoblasts," Frenkel said. "Once we understand that we can think about new therapeutic treatments for patients with chronic disease. The Baxter award gives us critical support toward reaching that goal."

Peter Brooks researches the process of angiogenesis — how new blood vessels form — and searches for biochemicals that block or promote that process. "The gift is going to help our project immensely. It's very generous and it came just at the right time," he said.

Brooks' research has already shed light on how the body's blood vessels construct new routes, especially at the prodding of tumors. He has helped to identify key vulnerabilities in that process, and targeting these, Brooks and his colleagues have developed agents with strong potential as new therapies for patients with cancer.

He will focus studies on a novel anti-angiogenesis drug, called PEX. "We want to find out more about how it works," he said.

The drug is a tiny fragment of an enzyme, called matrix metalloproteinase -2 (mmp-2). In its entirety, the mmp-2 enzyme promotes blood vessel growth. But the team has found that the PEX fragment shuts off angiogenesis and shrinks tumors. Working with David Cheresch of Scripps Research Institute and the company Merck KgaA of Darmstadt, Germany, Brooks plans to test the agent in patients.

In addition, Brooks is trying to figure out how PEX is naturally produced by the body. "If we knew that, we could stimulate the body to generate more."

—Eva Emerson

—Eva Emerson

# Calendar

## Monday, August 10

Noon. "Insulin Receptor Isoform A: A Newly Recognized IGF-II Receptor in Fetal Cells and Cancer," Chin Sung, USC. Norris Tower 7<sup>th</sup> Floor Conf. Ctr. Info: 442-1039

## Tuesday, August 11

8 a.m. Neurology Grand Rounds. "Headaches in the Emergency Room," Robert Cowan, USC. Univ. Hospital, Troy Room. Info: 226-2639

9 a.m. New Staff Orientation, KAM 308. Info: 442-1010

## Wednesday, August 12

7 a.m. Medical Grand Rounds. "Hemochromatosis," Donald Feinstein and James Brewer, USC. GNH 1645. Info: 226-7556

1:30 p.m. "Dominant-Negative Interference of TGF-Beta Signaling in Chondrocyte Differentiation: Role of Indian Hedgehog and Parathyroid Hormone Related Peptide," Rosa Serra, Vanderbilt Univ. BMT 407. Info: 442-1881

## Thursday, August 13

Noon. "5HT Signal Transduction in the Biological Clock: Role of the 5HT7 Receptor," Joseph Miller, Texas Tech Univ. BMT 407. Info: 442-1881

## Friday, August 14

11 a.m. Hematology Conference. "Thrombosis," Howard Liebman, USC. GNH 7441. Info: 865-3913

## Tuesday, August 18

8 a.m. Neurology Grand Rounds. "Stroke Emergencies: Part II," Mark Fisher, USC. Univ. Hospital, Troy Room. Info: 226-2639

9 a.m. New Staff Orientation, KAM 308. Info: 442-1010

## Wednesday, August 19

7 a.m. Medical Grand Rounds. "Hepatocellular CA," Telfer Reynolds and Christopher Wong, USC. GNH 1645. Info: 226-7556

## Thursday, August 20

Noon. Gastrointestinal and Liver Disease Seminar. "The Liver Sinusoidal Endothelial Cell and Organ Preservation Injury," Steven Strasberg, Washington Univ. AHC Aud., Room 102. Info: 442-5576

## Friday, August 21

11 a.m. Hematology Conference. "Principles of Anti-Coagulation," William McGehee, USC. GNH 7441. Info: 865-3913

## Tuesday, August 25

8 a.m. Neurology Grand Rounds. "Ion Channels and Seizures," Jong Rho, Univ. of Washington. Univ. Hospital, Troy Room. Info: 226-2639

Notice: Deadline for calendar submission is 4 p.m. Tuesday to be considered for that week's issue. Please note that timely submission does not guarantee an item will be printed. Send calendar items to *HSC Weekly*, DEI 2510 or fax to 442-2832, or e-mail to [hscwkly@hsc.usc.edu](mailto:hscwkly@hsc.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.*

## SHIH: Research showed link between neurotransmitter and aggression

Continued from Page 1

two different forms of MAO, and went on to show that the two forms, called A and B, fulfill different functions in the body.

In a 1995 *Science* article co-authored with USC researcher Kevin Chen, French biochemists Isabella Seif, Edward De Maeyer and others, Shih genetically engineered mice deficient in the MAO-A gene, and then demonstrated that the mice were abnormally aggressive.

"When this gene is missing, the animals fight more and are hyperactive," Shih said. Without MAO-A, the mice produced excessively high levels of serotonin, a critical neurotransmitter. Humans with abnormally high levels of serotonin have also been shown to be prone to rage and aggression.

The link between the MAO-A deficiency and violent behavior was also

bolstered by earlier studies of one Dutch family with a history of criminal behavior and defects in the MAO-A gene.

Besides providing concrete evidence for the link between levels of neurotransmitters and behavior, Shih's mice have since become a valuable model for better understanding how abnormal brain chemistry relates to behavior, mental illness and disease in humans.

Shih has since created mice who lack a gene for MAO-B. Her results clearly show the different functions of the two forms of the MAO enzyme. She has found that the MAO-B-deficient mice have increased levels of a brain chemical, phenylethylamine, which may be associated with bipolar disorder and other mental illnesses. Currently, she is further investigating how the lack of the enzyme changes mice behavior.

—Eva Emerson