

Keck School lauds donors whose gifts 'changed campus forever'

The Keck School of Medicine honored W. M. Keck Foundation Chairman and President Robert Day along with other top supporters at a dinner held in the Keith Administration lobby on Sunday, May 16.

Portraits were unveiled of Day and donors Harlyne Norris and Selim Zilkha, which are now permanently displayed in the Keith lobby.

Ryan also presented gifts of traditional academic hardwood chairs to the three as well as to David Lee, chair of the Keck School Board of Overseers, and Jim Lower, Keck School Overseer.

At the dinner, Dean Stephen J. Ryan thanked Day, Norris and Zilkha for gifts "that have changed the campus and Keck School of Medicine forever."

Ryan commented that the portraits, painted by artist Juan Bastos, create a sense of the history of the Health Sciences Campus. "Great medical schools such as the leading schools on the east coast have these 'halls of fame,' places that display portraits of people who have done great things for that school," said Ryan.

"In a very real way, Robert Day is the reason that we are all here today," said Ryan. "There would not be a Keck School of Medicine without Robert. At the end of the last century, Robert recognized the potential of our school and made an unprecedented gift and pledge of his support. In this century, he has remained an enduring, stalwart advocate for the school."

"Words are inadequate to describe all that he has done for us in the Keck School of Medicine," added Ryan. "I won't recite his extensive bio and all he has accomplished in the worlds of business and politics. I will tell you, however, that he is one of the most generous people anywhere, and a leading philanthropist. He provides inspired leadership for the W. M. Keck Foundation. The Keck Foundation is the most efficient and effective organization that I know, and a model in allocation of its resources with the

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Above, (front row, from left) Jim Lower, Selim Zilkha, Robert Day, Harlyne Norris, David Lee; (back row, from left) William Watson, Brian Henderson, Stephen J. Ryan, Peter Jones and Zach Hall are flanked by portraits that honor the Keck School of Medicine's top supporters.

Right, artist Juan Bastos with his portraits of Day, Norris and Zilkha.



Lee Salem Photography, Inc.



USC cancer researchers examine potential of epigenetics in *Nature*

Researchers from the USC/Norris Comprehensive Cancer Center heralded an entirely new approach to the treatment of aging, inherited diseases and cancer in a review paper published in the May 27 issue of the journal *Nature*.

Dispelling the belief that the only way to treat such conditions is by fixing or replacing damaged genes, they instead focused on the field of epigenetics—the study of changes in gene silencing that occur without changes in the genes themselves.

Many genes in our bodies are permanently

turned off as part of normal development. But sometimes that process goes awry, turning off genes that should otherwise remain active. The new field of epigenetic therapy, put forth by the USC researchers in their *Nature* review paper, aims to switch these genes back on.

In their article, Peter Jones, director of USC/Norris and Distinguished Professor of Biochemistry and Molecular Biology and Urology at the Keck School of Medicine, and his colleagues laid out their new perspective on the treatment of

genetic disorders by discussing the potential ways to interfere with epigenetic gene silencing, and the ways in which that potential is already being exploited.

"The fact that many human diseases, including cancer, have an epigenetic etiology has encouraged the development of a new therapeutic option that might be termed 'epigenetic therapy,'" Jones and his colleagues wrote. They added that a number of chemical compounds have been found that have an

See **JONES**, page 4



From left, Stephen J. Ryan, Jeffrey Huffman, Dale Garell and Steven Sample help dedicate the HCC II on May 21.

Lee Salem Photography, Inc.

USC celebrates opening of \$49-million HCC II patient care building

A new era in health care was the recurring theme at the ribbon cutting for the Healthcare Consultation Center II (HCC II) on May 21.

Attended by more than 150 people, the event marked the official opening of USC's newest and largest building.

The \$49-million, 238,000-square-foot medical office building is located on San Pablo Street at the entrance to the Eamer Medical Plaza.

USC President Steven B. Sample, Dean Stephen J. Ryan, USC Care Medical Group President and CEO Jeffrey Huffman, and USC Care Medical Group Chair of the Board Dale Garell participated in the ceremonial ribbon cutting.

"Today is particularly meaningful for me as Dean of the Keck School of Medicine," said Ryan in his remarks preceding the ribbon cutting. "To see yet another milestone come to fruition and see another of the school's dreams realized is very rewarding.

"What the faculty members do here every day is the very heart of academic medicine: scientists searching for cures to devastating diseases, doctors performing life-saving procedures not offered in a community setting, educators teaching and mentoring a future generation of physicians and scientists. It is buildings like HCCII where that all comes to life. But while buildings such as

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Keck School of Medicine students rack up impressive academic gains

With the closing of another academic year, Keck School of Medicine of USC leaders are applauding educational gains made by students and efforts undertaken by faculty members in 2003-2004.

Students logged their highest average scores yet on medical licensing exams during the school year. Their classmates successfully navigated the school's new medical curriculum. And that academic excellence was contagious: Medical College Admissions Test (MCAT) scores and undergraduate grade point averages (GPAs) for students entering the Keck School are reaching new highs.

"I take tremendous pride in our students and their accomplishments. The students who have worked with our previous curriculum and those who have worked with the new curriculum have all done a spectacular job," said Keck School Dean Stephen J. Ryan. "I have been so impressed with how well the students have worked with the faculty in developing this curriculum.

"I personally believe that our new curriculum is at the very forefront of medical education. I salute the students and the faculty on this tremendous accomplishment,"

Capping off the year, the Keck School rose in stature in *U.S. News and World Report's* 2004 "Annual Guide to Best Graduate Schools" rankings. The Keck School of Medicine ranked 32nd for top medical schools, a three-place improvement from the 2003 rankings, and an 11-place improvement since 2001.

A big part of the improvement came from the school's overall student selectivity ranking, which rose 42 places since 2001. Student selectivity is based on MCAT scores, GPA and acceptance rates.

GPA for entering students in 2003 was 3.62, higher than the 3.50 mark in 1999 and significantly higher than the 3.40 mark set in 1993. And signs are good for the incoming class, academic officials reported: The new entering class's average GPA is 3.65.

MCAT scores are also up. The class entering in 2003 scored an average of 32.4, up from 31.5 in 1999 and 29.4 in 1993. This fall's entering class has higher MCAT scores still, averaging 33.1.

The qualifications of entering students is just part of the story, however. Students who have spent the last few years at the Keck School learning under the new curriculum are demonstrating academic excellence.

Allan V. Abbott, associate dean for curriculum and continuing medical education,



Ite A. Laird-Offringa, assistant professor of surgery and biochemistry, hoods master's degree recipient Cindy Lin at the Keck School's commencement ceremony.

explained that the new curriculum is designed to enhance the understanding and clinical relevance of the basic sciences, as well as to improve students' problem-solving and independent study skills. The new curriculum also is based on the use of real patient cases and increasingly incorporates small-group learning, directed self-study and new learning technologies.

Students also participate in a major new mentoring program, called Professionalism and the Practice of Medicine, in which meet weekly with senior faculty members to build professionalism and create a sense of collegial community; working in small groups, they address issues including communication skills, ethical judgment and the social and community contexts of health care.

After completing their first and second years under the new curriculum, third-year students achieved the school's highest average scores on the United States Medical Licensing Examination (USMLE) Step 1 test. These students, who will graduate in spring 2005, were the first to go through the Keck School's revised curriculum.

The National Board of Medical Examiners requires that medical students pass the USMLE's three steps of tests to become practicing physicians in the U.S. and Canada. Students take the Step 1 test after their second year of medical school.

In addition, clinical faculty members reported that the third-year students were well-prepared for their required clinical clerkships.

Abbott congratulated faculty members for the gains.

"During the first three years of new curriculum implementation, the faculty has exhibited a remarkable dedication to the education of medical students despite other mounting pressures," Abbott said.

He noted that as the Keck School strives to improve its standing in garnering medical research dollars, faculty members face mounting time demands to carry out research projects. At the same time, clinical faculty members have seen their practices become increasingly complex while clinical revenues decrease.

"It is a tribute to these faculty members that they have continued to find ample time and energy to devote to the enhancement of the educational process of our medical students," he said.

Clive R. Taylor, senior associate dean for educational affairs and professor and chair of pathology, praised the role the Keck School Admissions Office has played in recruiting students and bringing top candidates to campus. "This has become a very active, rather than just a passive, process," Taylor said.

In 2001, admissions officials developed a new strategy and goals for recruitment. They publish an attractive admissions viewbook, regularly visit the top undergraduate universities, build relationships with pre-medical advisors at the universities and hold information sessions for students over the summer, for example. In the past two years, they have made 30 visits to undergraduate schools and pre-medical fairs all over the country; in previous years, most visits were restricted to California.

They also mail personal letters and information packets to selected, highly qualified applicants at the beginning of each application cycle. In addition, they hold annual "accepted student receptions," in which they invite accepted students to revisit campus, shadow faculty members in the clinics and labs and talk with Keck School students and faculty members.

Perhaps the greatest reflection of the campus's educational mission lies within the experiences of the students themselves. Deborah Trujillo, who graduated with her Keck School classmates in commencement exercises on May 16, is one example.

Trujillo, from Irvine, will be doing her internship in internal medicine at the University Medical Center in Las Vegas and will finish her residency in emergency medicine at the University of Alabama, Birmingham.

She praised the commitment and caring of

all of her teachers at the Keck School, especially Alexandra M. Levine, Distinguished Professor of Medicine, chief of hematology and Ronald H. Bloom Family Chair in Lymphoma at the Keck School of Medicine. "She is the best role model I can think of when it comes to a physician who will go completely out of her way in order to help," Trujillo said. She noted that every one of her instructors has helped mold her medical future in some facet or form.

"We were once told very early on in our medical school careers that we would not appreciate our education until we left USC," she said. "I cannot tell you how true a statement that really is . . . Yes, there are many educators that stand out above the others, but I enjoyed working with them all and know in whatever way, they all played a role in making me the doctor that I am going to become."

—Alicia Di Rado

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• **Emergency Information**
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The emergency telephone system can handle 1,400 simultaneous calls. It also has a backup system on the East Coast.

HSC Weekly

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Newsmakers

A May 27 *Forbes* magazine Web site story looked at the viability of using decades-old sperm to produce babies. The story quoted fertility expert **Richard Paulson** and also appeared on Yahoo News, dr.Koop.com and *Health Day News*.

On May 26, the Univision television network (Channel 34 in Los Angeles) aired a story on the USC/Norris CyberKnife. The story included radiation oncologist **Parvesh Kumar**.

A May 26 *Los Angeles Times* story on aspirin and breast cancer quoted USC/Norris oncologist **Christy Russell**.

A May 25 *Sacramento Bee* story on tobacco products on campuses quoted researcher Tess Boley Cruz. Cruz was also quoted in a similar story in the May 22 *Fresno Bee*.

A May 23 *Milwaukee Journal Sentinel* story looked at pacemakers and defibrillators. The story quoted cardiologist **Leslie Saxon**.

On May 19, KPCC-FM radio ran a story on tobacco researcher **Jennifer Unger's** study showing teens whose parents lose jobs smoke more. The story also ran on the City News Service, Medical News Today, KCSN-FM and TV-station Web sites around the country.

HSC Research Grants for April 2003

DEBORAH L. COMMINS, ROSCOE ATKINSON
Pathology
Sponsor: University of California, Los Angeles
“National Neurological AIDS Bank (NNAB)”
\$88,395

MARTHA L. CRUZ
Preventive Medicine
Sponsor: National Institute of Diabetes & Digestive & Kidney Diseases
“Prevention of Diabetes in Obese Hispanic Adolescents”
\$325,100

ROBERT W. HAILE
Preventive Medicine
Sponsor: Stanford University
“Breast Cancer Risk Modifiers in BRCA Mutation Carriers”
\$51,343

ANN HAMILTON
Preventive Medicine
Sponsor: National Cancer Institute
“Racial/Ethnic Differences in the SF-36 Outcome Measures Through 5 Years of Follow-Up”
\$19,954

SARAH HAMM-ALVAREZ, AUSTIN K. MIRCHEFF, JOEL E. SCHECHTER, AUSTIN YANG
Pharmacy
Sponsor: National Eye Institute
“Microtubule-Based Transport in Lacrimal Gland Function”
\$1,709,000

SUE INGLES
Preventive Medicine
Sponsor: University of California, Los Angeles

“Genetics, Obesity and Breast Cancer Risk”
\$205,944

SUE INGLES
Preventive Medicine
Sponsor: National Institute of Child Health and Human Development
“A Pilot Study of Novel Candidate Genes for Preeclampsia”
\$446,719

BRENDA JONES, PATRICIO ESCALANTE
Medicine
Sponsor: University of California, San Diego
“Tuberculosis Curriculum Coordinating Center (TCCC)”
\$775,000

W. MARTIN KAST
Cancer Center
Sponsor: National Cancer Institute
“VLP Vaccines Against HPV-Induced Tumors”
\$976,719

HEINZ-JOSEF LENZ
Cancer Center
Sponsor: University of California, Davis
“Simultaneous Care: Linking Palliation to Clinical Trials”
\$155,016

ALICIA A. MC DONOUGH
Physiology and Biophysics
Sponsor: National Institute of Diabetes & Digestive & Kidney Diseases
“Regulation of Sodium Pumps in the Kidney”
\$1,797,427

GISELLE PETZINGER
Neurology

Sponsor: U.S. Army Medical Research and Materiel Command
“Pharmacological and Behavioral Enhancement of Neuroplasticity in the MPTP-Lesioned Mouse and Non-Human Primate”
\$1,880,720

STEPHEN A. STOHLMAN
Neurology
Sponsor: National Institute of Allergy and Infectious Diseases
“Regulation of Gender-Dependent EAE Susceptibility”
\$324,750

HIDEKAZU TSUKAMOTO
Pathology
Sponsor: National Institute of Alcohol Abuse and Alcoholism
“Center for Alcoholic Liver and Pancreatic Injury”
\$1,629,366

J.P. VAN DER MEULEN, THOMAS BUCHANAN, FRED SATTLER, RICHARD M. WATANABE
Medicine
Sponsor: National Center for Research Resources
“General Clinical Research Center”
\$8,177,602

JEFFREY S. WEBER
Cancer Center
Sponsor: University of Washington
“Immunologic Correlates of Effective Immunization for Cancer Vaccines”
\$7,773

JIAN-MIN YUAN, RONALD K. ROSS, MIMI YU
Preventive Medicine
Sponsor: National Cancer Institute
“Dietary Factors in the Etiology of Colorectal Cancer”
\$1,668,188

HCC II: Patient-focused design was key

Continued from page 1
this one are great—and they truly are—it is the people inside those buildings, the patients, the doctors and the other important members of the patient care team, that are what this place is all about.

“Those people, with this great new facility to call home, are the future of the Keck School of Medicine—and that future is very bright.”

Huffman spoke about the vision behind the HCC II.

“When we began to envision our new patient care facility, we started with a simple concept: That every detail of this building would be focused on how to best serve our patients,” said Huffman. “I’m proud to say today we have realized our goal in the Healthcare Consultation Center II.”

In addition to citing the university and Dean Ryan, Huffman also credited the faculty for HCC II. “It was their commitment to their patients, combined with their hard work, that made this building possible. It is great to know that they

have this wonderful new facility to now call home,” Huffman said.

During his remarks, President Sample announced a major gift naming the HCC II’s outdoor plaza, where the event was taking place.

“I have the pleasure today of announcing that the plaza upon which we have gathered will be named for a great Trojan family—the Kennedys,” said Sample. “USC has benefited from this family’s support for nearly five decades. Jack Kennedy Jr. was a varsity swimmer for USC in 1955-1956, and he and his wife, Nancy, have been loyal Trojans ever since.

“Their son Jack Kennedy III is also an alumnus, and he and his parents provided the naming gift for the Kennedy Family Aquatics Building on the University Park campus. Ladies and gentlemen, welcome to the Kennedy Family Plaza.”

Following the ribbon cutting, guests toured the building’s five patient care levels.

—Brenda Maceo

CHLA creates imaging-compatible incubator

Researchers from Childrens Hospital Los Angeles (CHLA) and the Keck School of Medicine have pioneered a magnetic-resonance (MR) compatible incubator that will allow radiologists to safely and efficiently obtain quality diagnostic images of sick infants. An article describing the incubator and its utility appears in the May issue of the journal *Radiology*.

“Magnetic resonance imaging is the most desirable imaging test for many newborns, because there is no exposure to radiation,” said Stefan Bluml, research scientist at the Saban Research Institute of CHLA, associate professor of radiology at the Keck School and lead author on the paper.

“However, many sick newborns cannot be studied by MR, even when clinically indicated, because of concerns for their safety during transport and during the procedure.”

There are considerable challenges in providing good diagnostic images of newborns, some of which include monitoring their circulation and maintaining constant control of temperature, airflow and humidity. Consequently, few newborns are examined with MR imaging, which is, for many indications, the most accurate non-invasive diagnostic test. Unlike X-rays and CT scans, MR imaging involves no radiation risk.

“The MR-compatible incubator streamlines the MR examinations of newborns and allows the nursing staff to do most of the patient preparation inside the safe environment of the hospital’s neonatal intensive care unit,” Bluml said.

The researchers conducted 13 MR imaging studies to evaluate the MR-compatible incubator with air temperature and humidity regulation and integrated radio-frequency coils. They found that the quality of the images they obtained were superior to those obtained with standard MR equipment.

The customized small coils used with the MR-compatible incubators reduce scan time and improve image resolution, Bluml explained. Typically, MR imaging exams of infants are performed with the manufacturer’s one-size-fits-all coils, which are designed for adult heads.

Bluml is hopeful that this new technology will allow MR studies of newborns that will result in earlier and improved diagnoses and enable early intervention and treatment. He said he also believes that the incubator’s safe environment will enable more neonatal clinical research.

Said Bluml: “We believe that magnetic resonance compatible incubators are beneficial for babies and will be cost effective in the long run.”

Collaborating with Bluml were Keck School and Saban Research Institute researchers Philippe Friedlich, Stephan Erberich, John C. Wood, Istvan Seri and Marvin D. Nelson Jr.

PORTRAITS: Keck School unveils artistic tribute to top supporters

Continued from page 1

most minimal administrative costs. Robert has always been clear about his desire to do something great for Los Angeles.

"The Keck gift launched our ambitious plans and dreams and propelled the Keck School of Medicine into the top echelon of our nation's medical schools.

"In good times and bad, Robert Day has repeatedly demonstrated his unwavering commitment, and for that I thank him on behalf of our entire faculty, student body, staff and the leadership of the school."

Ryan also recounted the contributions of Harlyne Norris and the Norris family and foundation.

Through its foundation, the Norris family has given more than \$40 million to USC, naming the USC/Norris Comprehensive Cancer Center, the Eileen L. Norris Cinema Theater, the Norris Dental Center, the Norris Medical Library and the Norris Auditorium, which is on the University Park Campus.

Harlyne Norris has served on the Norris Cancer Hospital Board, is a dedicated member of the USC Board of Trustees and has been called the "heart and spirit" behind the new Harlyne J. Norris Cancer Research Tower, which is now under construction.

The Norris Foundation provided a \$15-million lead gift for the tower.

Ryan also lauded Zilkha as a crucial benefactor and "a truly outstanding man."

"I feel privileged to call Selim Zilkha my friend," Ryan said. "He has had so many lives in industry and has reinvented himself many times from banking to services for pregnant women through MotherCare, to the oil business and renewable energy, and more recently, developing successful vineyards with his daughter, Nadia. Selim made the neurogenetic institute possible, a place where researchers can address the devastating diseases of the brain, which have such a measurable impact upon the health of our aging population."

Others attending the event from the Keck

School included Brian Henderson, incoming dean and director of the Zilkha Neurogenetic Institute, Peter Jones, director of the USC/Norris Comprehensive Cancer Center, and Zach Hall, executive vice dean and senior associate dean for research.

Ryan praised them for their leadership of the school.

"People make us who we are," said Ryan, "We are most fortunate that three of our greatest faculty leaders and scientists are with us tonight. The leadership of Brian Henderson has been outstanding, as a great founding director of the Zilkha Institute and previously as director of the Norris Cancer Center. He will be a great dean. Zach Hall has done an outstanding job in leading the Keck School's research efforts and also carrying a huge administrative load since October, serving as executive vice dean.

"We will always be indebted to Zach for joining us. His commitment to high quality is legendary at UC San Francisco and at the NIH,

where he held major leadership roles. He is building a true community of scholars and scientists here. Together, Brian and Zach are in the midst of exciting recruitments for the Zilkha Neurogenetic Institute," Ryan said.

He added: "Peter Jones has also done a spectacular job in recruitment and leadership from the time he succeeded Brian Henderson to become director of Norris, providing visionary leadership for the Cancer Center."

In remarks at the end of the evening, Day indicated how proud he was to have become a part of the medical school, the privilege of working with Ryan and how he still believes firmly in the future of the Keck School of Medicine.

Earlier in the day, at the Keck School commencement exercises, Ryan presented Day with the Hoffman Award, honoring the individual who has made the greatest contributions to the Keck School of Medicine and its people.

"Without doubt," said Ryan, "Robert Day is that person."

JONES: Importance of epigenetic therapy drug is hard to overstate

Continued from page 1

effect on some form of epigenetic gene change, and noted that "several of these agents are currently being tested in clinical trials," including trials conducted at USC/Norris.

This *Nature* review came just days after the U.S. Food and Drug Administration (FDA) approved the epigenetic inhibitor azacitidine (Vidaza™, Pharmion Corporation) for the treatment of a pre-leukemic bone-marrow disorder known as myelodysplastic syndrome, or MDS.

MDS, which is characterized by the production of abnormal, immature blood cells, affects between 10,000 and 30,000 people each year, is most prevalent in people over age 60, and can be fatal. Until now, there was no approved treatment for MDS.

Azacitidine was first synthesized in the 1960s in Czechoslovakia; it received its first exposure in the United States in the Childrens Hospital Los Angeles laboratory of then-fellow Peter Jones.

Although the drug had initially been envisioned as a chemotherapy agent, Jones showed that it had great utility in the laboratory because it could turn on genes that had been previously locked down by methylation—a type of epigenetic change in which a methyl group becomes physically attached to the region of a gene that regulates its production of protein, shutting it down.

But Jones, who is one of the world's pre-eminent epigenetics experts, said that azacitidine's approval is bigger than its role in MDS.

"This is the first approved drug in a new kind of therapy—epigenetic therapy," Jones noted. "That gives it

tremendous potential importance not just in this disease, but in a host of others as well."

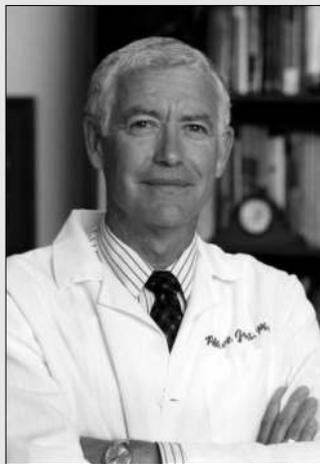
Indeed, cancer and its relatives are far from the only conditions that may be affected by epigenetic gene silencing, Jones noted. A number of other diseases—most notably several that can lead to intellectual disabilities—appear to have epigenetic roots. Among them are Fragile X syndrome, Angelman syndrome, Prader-Willi syndrome and Rett syndrome. Jones also sees the application of epigenetic therapy to combat disorders caused by aging, providing the opportunity to turn on genes shut down by the aging process.

The search for the right drugs to undo the epigenetic damage as wide-ranging as their possible targets. Jones is involved in research into the utility of a compound called azadeoxycytidine—a more specific version of azacitidine that only affects DNA and thus potentially carries fewer side effects. Many of the

major pharmaceutical companies have at least one methylation inhibitor trial ongoing, Jones added, and there are dozens of additional compounds being screened for their potential utility.

"It is apparent that we are just at the beginning of understanding the substantial contributions of epigenetics to human disease, and there are probably many surprises ahead," Jones and colleagues noted in their review. "Elucidating the whole bandwidth of epigenetic mechanisms is an exciting challenge and will eventually lead to a clearer understanding of the development of human disease and lead therapeutic concepts into new directions."

—Lori Oliwenstein



Peter Jones

Calendar

Wednesday, June 2

7 a.m. Medicine Grand Rounds. "TTP," Anil Tulpule, USC. GNH 1645. Info: 226-7591

Sunday, June 13

3 p.m. "Coping with Methuselah, Long Range Planning for Quality Life," William Schwartz, USC. CSC, IGM Aud. Info: (310) 479-1827

Notice: **Deadline for calendar submission is 4 p.m. Tuesday** 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, DEI 2510 or fax to (323) 442-2832, or e-mail to lpatt@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.

The HSC Calendar is online at
<http://www.usc.edu/hsccalendar>

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HSC Weekly has begun its summer publication schedule and will appear approximately every other week through mid-September.