

Published for the Students & Employees of the USC Health Sciences Campus

**New CHLA-USC program offers innovative** 

care to high-risk pregnancies

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**JANUARY 16, 2009** 

## USC study uncovers shortcomings in care for advanced liver disease

### By Meghan Lewit

A recent study conducted at the Keck School of Medicine and nine other clinical centers around the country found that treating patients who have chronic hepatitis C and advanced liver disease with longterm pegylated interferon significantly decreased their liver enzymes, viral levels and liver inflammation, but the treatment did not slow or prevent the progression of serious liver disease.

These findings come from the clinical trial, Hepatitis C Antiviral Long-Term Treatment Against Cirrhosis (HALT-C) and were reported in the *New England Journal of Medicine* in December.

"An important aspect of the results of the HALT-C study is that this is obviously a very difficult population to treat because of the resistance of their viral infection to the currently available treatment," said Karen L. Lindsay, professor of medicine at the Keck School and the principal investigator from USC on the study. "One in three patients in the study developed advanced problems with liver function over a three-year period clearly demonstrating that patients with hepatitis C and liver fibrosis are at high risk for developing severe problems with liver function."

Current standard of care therapy for chronic hepatitis C viral infection is a course of pegylated interferon injections and oral ribavirin therapy for up to 48 to 72 weeks, with a goal of eradicating the infection when treatment is discontinued. But patients who do not have a sustained response to initial therapy have been given peginterferon alone over a longer time. Small studies have shown that this approach suppresses viral and enzyme levels, even if the virus is not completely eliminated. However, it was not known if longterm therapy would improve important clinical outcomes such as liver damage and death.

"The results from HALT- C show without question that maintenance therapy with pegylated interferon does not prevent progression of liver disease among patients who have failed prior treatments," said James Everhart, project scientist for HALT-C in the Division of Digestive Diseases and Nutrition, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the principal sponsor of HALT-C at the National Insitutes of Health (NIH). "These findings heighten the incen-

### ge and Fadiman received critical acclaim for her

Auditorium.

first book, "The Spirit Catches You and You Fall Down," which chronicles the cultural barriers between an epileptic Hmong child and her family and the medical establishment in Merced, Calif.

weekly

By Cheryl Bruyninckx

risk pregnancies.

A new fetal therapy program,

Childrens Hospital Los Angeles, is now providing innovative pro-

cedures for women with high-

The CHLA-USC Fetal

Institute for Maternal Fetal

Therapy Program is part of the

Health. Ramen Chmait, director of the CHLA-USC Fetal

Therapy Program, is one of a few

surgeons west of the Mississippi

who can perform specialized fetal surgery to treat conditions while

the baby remains inside the

womb. Chmait is also assistant

professor of clinical obstetrics and

gynecology, division of maternal-

fetal medicine at the Keck School.

ration, women with high-risk preg-

nancies have new options," he said.

"Through this important collabo-

A wide variety of fetal abnormali-

ties can be treated through fetal sur-

Transfusion Syndrome-a rare con-

dition seen in approximately 10 per-

placenta. The condition is caused by

an unbalanced flow of blood through

As fetuses share the same placen-

**BEYOND THE SCIENCE OF DISEASE**— Author and essayist Anne Fadiman (at left) was the special guest for a lecture on cul-

tural sensitivity, illness and the practice of medicine, which was part of USC's Visions

and Voices initiative, held Jan. 12 in Mayer

cent of twins who share the same

vascular channels that connect the

circulatory systems of each twin

through the common placenta.

gery, including Twin-Twin

created by the Keck School of Medicine of USC, Hollywood

Presbyterian Hospital and

Speaking to a packed room, Fadiman urged students to look beyond the science of disease. "Illness is not objective, it is subjective," she said. "What you see will be entirely different than what the patient sees."

Fadiman was joined by Raquel Arias (at right), associate dean for Educational Affairs at the Keck School, for a special question and answer session following the lecture. Arias was an obstetrician in the Merced clinic in the 1980s and is featured in Fadiman's book.



Patient Jody Madden and her two healthy babies pose with Ramen Chmait, the doctor who performed fetal surgery to treat Twin-Twin Transfusion Syndrome.

ta, blood flow to each twin becomes unequal. One fetus becomes overloaded with amniotic fluid and can develop heart failure, while the other —deprived of amniotic fluid—may develop low blood volume. In these situations, when left untreated, there is over a 90 percent chance neither baby will survive.

With the help of new technology, Chmait can perform fetal surgery on new mothers diagnosed with Twin-Twin Transfusion Syndrome. A three-and-a-half-millimeter scope allows surgical access into the womb with minimal disturbance to the pregnancy and the mother. The surgery is performed under local anesthesia through an incision that is less than half of one centimeter.

"Fetal surgery gives women with high-risk pregnancies, such as Twin-Twin Transfusion Syndrome, hope," said Chmait. "I quote my patients about a 90 percent chance that following this procedure at least one baby will survive and 72 percent chance that both babies will survive."

For more information, please call the Institute for Maternal Fetal Health at (323) 361-6074 or visit www.maternal-fetalhealth.org.



## Pharmacy reseacher studies lung damage in former smokers

Even after they stop smoking, patients with chronic obstructive pulmonary disease continue to experience lung damage.

Enrique Cadenas, the Charles Krown Alumni Professor in Pharmaceutical Sciences and associate dean for research affairs at the School of Pharmacy, has received a grant of \$394,380 over three years from the Tobacco-Related Disease Research Program to study emphysema associated with chronic obstructive pulmonary disease.

The study examines the observation that apoptosis, or cell death, continues to occur in patients with the disease even after they have stopped smoking. Cadenas will explore the idea that once mitochondria are damaged by smoking, a vicious cycle is unleashed that spreads and intensifies the already damaging effects of cigarette smoke.

"This impairment of mitochondrial function ultimately causes cell death, which often leads to emphysema," Cadenas said. "During the course of the project, we will consider compounds that can offset this destruction by improving mitochondrial function and thus halt or minimize the damaging effects of past smoking."

Chronic obstructive pulmonary disease damages and obstructs the lung airways, making it hard to breathe. Cigarette smoking is commonly associated with the disease, causing more than 90 percent of the cases. It is estimated that more than 24 million Americans have the disease, many of them undiagnosed.

The Tobacco-Related Disease Research Program was created in California in 1989. Funded by cigarette surtax revenues, the program supports research projects on tobacco-related diseases.

Cadenas is known for his work on cellular dysfunction in the aging process and age-related, degenerative diseases. His work considers events that produce free radical injury and the development of therapeutic models that prevent free radical damage and the effects of aging.

# **USC's nanoscience initiative rolls threes**

#### By Carl Marziali

The biomedical nanoscience initiative at USC marked its third anniversary with a pair of notable threes: the attainment of full operational status for three core laboratories and the recruitment of three prolific young researchers.

Research on the nanometer scale—on the order of billionths of a foot—holds particular promise for medicine, because nanoparticles are small enough to circulate in the body but not so small as to vanish quickly into the waste stream. Biomedical nanoscience aims to use nanoparticles for new diagnostic tests and treatments.

At their recent annual meeting, USC faculty involved in the initiative compared notes, heard presentations from their peers and external speakers, and assessed progress to date.

Richard Cote, professor of pathology and urology in the Keck School of Medicine, co-chair of the initiative along with Mark Thompson of USC College, highlighted recent achievements from his and Thompson's interdisciplinary research group, which also includes Chongwu Zhou of the USC Viterbi School of Engineering.

"This has been a very successful effort that has resulted in publications and major grant funding," Cote said.

Funding for the group from federal agencies and private foundations over the past three years totaled more than \$8 million to Cote's group, in collaboration with Thompson and Zhou at USC, Y.C. Tai at the California Institute of Technology and others.

More importantly, the group's research has led to clinical trials for treatments of prostate cancer with a microfilter that traps tumor cells, and for a new nanoscale method to detect bladder cancer.

"This has resulted in a whole series of patents and patent filings," Cote said. The group has formed two companies to translate the research into real-world clinical treatments.

### CORRECTION

In the Jan. 9 issue of *HSC Weekly*, Irene Golden is pictured with Keck School Dean Carmen A. Puliafito. She was misidentified as Irene West. The *HSC Weekly* editorial staff apologizes for this error. Randolph Hall, vice provost for research advancement, reminded the group that biomedical nanoscience is one of USC's primary research emphases. To that end, Executive Vice President and Provost C. L. Max Nikias has invested in the creation and upgrade of core laboratories to support the initiative.

The university now maintains six core labs under the nanoscience umbrella: cell and tissue imaging, nanobiophysics, nanoimaging, nanofabrication, nuclear magnetic resonance and proteomics.

Three of the labs are fully operational, with the rest expected to follow in the near future.

The nanobiophysics core, established in 2007, already has served 19 research groups in five schools, said director Xiaojiang Chen, a structural biologist at the College. The new instruments helped Chen's group to describe an anti-HIV protein in a study published this year in the journal *Nature*.

A group led by Zhou and Richard Roberts, a chemist at the College, along with Thompson and Cote, has used the core's instruments to design methods for the possible detection and treatment of the SARS virus and other pathogens.

The cell and tissue imaging core has added \$1.3 million of instrumentation over the past year, including a scanning electron microscope, a transmission electron microscope and a live cell imager, according to lab manager Ernesto Barron.

The new proteomics core is dedicated to the identification and study of proteins. Associated mostly with food in the public mind, proteins are omnipresent in the body as the products of gene expression, disease and immune response.

The exact role of most of the one million proteins in the body remains unknown, said Ebrahim Zandi of the

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Richard Cote, co-chair of the biomedical nanoscience initiative at USC

Keck School of Medicine, who directs the proteomics core.

Since opening in September, the core already has served 10 research groups and has supported several pending proposals for large-scale proteomics projects.

"We're very pleased with the outcome from these investments," Hall said.

The other part of the provost's investment is in young talent.

The initiative has sponsored three new hires: Andrea Armani of USC Viterbi studies optical sensing of medically significant molecules; Alex Benderskii, a physical chemist coming to USC College in the fall of 2009, uses lasers to study variations in molecule shapes and functions; and Julio Camarero of the USC School of Pharmacy (see page 4) is developing ways to improve the sensitivity of diagnostic microsensors by ensuring that any "soft" matter on the sensors, such as proteins, does not lose key properties when it is attached to the hard chip underneath.

The highest remaining priority, Hall said, is the recruitment of additional senior faculty to provide research leadership and attract more students and researchers.

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# weekly

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### Next Issue: January 30

Senior Vice President, University Relations: Martha Harris Contributors: Eva Blaauw,Cheryl Bruyninckx, Veronica Jauriqui, Meghan Lewit, Carl Marziali and Kukla Vera

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## Panel to discuss value of emotional intelligence in teaching

#### By Sara Reeve

Emotional Intelligence (EI) can be defined as the ability to identify, understand, use and manage emotions in self and others.

"Generally speaking, emotional intelligence improves an individual's social effectiveness. The higher the emotional intelligence, the better the social relations," said Win May, associate professor and director of the standardized patient program in the division of medical education in the Keck School of Medicine. "When it comes to the question of whether a person will become a star performer, IQ may be a less powerful predictor than EI."

Navigating emotional information can be hazardous, but the USC Center for Excellence in Teaching will provide faculty, staff and students the opportunity to learn about the value of EQ from three distinguished professors.

The panel discussion, which will be held on Jan. 28 at noon in the Keith Administration Building, Room B21/23, will feature May; J. Lawford Anderson, professor of earth sciences and director of the Center for Excellence in Teaching; and Frank Manis, professor of psychology.

"Lapses in EI can lead to 'plateaued' or derailed careers," said Anderson. "The great thing is that it can be learned through interactions with others."

For more information, call (213) 821-3925 or visit

www.usc.edu/programs/cet/calendar.

## HALT-C: Study has changed clinical care for chronic hepatitis C patients

#### Continued from page 1

tive to develop more effective drugs for patients with severe liver disease due to hepatitis C."

HALT-C, a randomized multicenter trial of 1,050 patients with chronic hepatitis C who had failed prior treatment to eradicate the infection, tested

whether long-term treatment with pegylated interferon alfa-2a would reduce the development of cirrhosis, liver cancer or liver failure.

The 517 patients randomized to the treatment arm received 90 micrograms of pegylated interferon in weekly injections for 3.5 years. The 533 patients in the control arm underwent the same follow-up and care as the treated

patients including liver biopsies, quarterly clinic visits and blood tests. All patients had advanced liver fibrosis, a gradual scarring of the liver that puts patients at risk for progressive liver disease and liver failure.

The outcomes studied in HALT-C were death, liver cancer or liver failure, and for those who did not have cirrhosis initially, the development of cirrhosis.

At the end of the study, 34.1 percent of the treated group and 33.8 percent of the control group had experienced at least one of the studied outcomes. Patients in the treated group had significantly lower blood levels of the hepatitis C virus and improvement in liver inflammation. However, there was no major difference in rates of any of the primary outcomes between the groups. Among treated patients, 17 percent

stopped pegylated interferon after 18 months and 30 percent stopped the

drug after two years. Known interferon side effects were the most common reason for stopping the drug.

"The study was highly productive and important because it was the first long-term prospective study of patients with advanced hepatitis C," Lindsay said. "Numerous ancillary studies were included as part of the overall project, which

is currently in its tenth year. The results of these data analyses have already led to more than 30 publications on this patient population and many of these results have changed the standard of clinical care for such patients."

Karen L. Lindsay, principal investigator

of the HALT-C study

The hepatitis C virus infects more than 170 million persons worldwide and as many as four million in the United States. Hepatitis C ranks with alcohol abuse as the most common cause of chronic liver disease and is the leading cause for liver transplantation in the United States.

The best current antiviral therapy of

### ETCETERA

**Robert K. Rude**, professor of medicine, was presented with the American College of Nutrition's Alexander & Mildred Seelig Magnesium Award at the organization's annual meeting in October. Rude was recognized for his work researching the link between magnesium deficiency and osteoporosis.

Marvin E. Belzer, head of the division of adolescent medicine at

Childrens Hospital Los Angeles and associate professor of pediatrics at the Keck School of Medicine, has been appointed to a two-year term as Subboard Chair for Adolescent Medicine (2009-10) by the American Board of Pediatrics. Belzer's duties will include administrative and editorial responsibilities. pegylated interferon given by injection in combination with oral ribavirin for about 6 months to a year eliminates the virus in about 50 percent of infected patients.

The magnitude of the HALT-C study demonstrates the importance of collaboration in clinical research, Lindsay noted.

Of the clinical centers that participated, USC was third in the number of patients enrolled and numerous Keck School faculty and their staff provided key support for the study.

HALT-C was funded by the NIH with additional support from Hoffmann-La Roche Inc.

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USC President Steven B. Sample

### Sample to present State of the School address Feb. 10

USC President Steven B. Sample will present his annual State of the School address on Tuesday, Feb. 10, in the Aresty Auditorium, Harlyne J. Norris Cancer Research Tower.

A reception will begin at 4 p.m., followed by the address at 4:30 p.m.

Sample became the 10th president of USC in March 1991. He is the university's first holder of the Robert C. Packard President's Chair.

# USC EMPLOYEES

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# **Calendar of Events**

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

#### Tuesday, Jan. 20

**11** A.M. "The U.S. Constitution and African Americans," Robert Penny, USC. HMR 100. Info: (323) 442-2806

**11:30** A.M. Psychiatry Grand Rounds. "Acute Psychosis and Coma in a 10-Year-Old Boy: Diagnostic and Treatment," Drs. Pataki, Rozenblat and Dopheide, USC. ZNI 112. Info: (323) 226-5572

#### Wednesday, Jan. 21

**4 P.M.** Research Workshops 2009. "Grant Opportunities and Proposal Development in the Humanities," Peter Mancall, USC. UPC: CUB 329. Info: ((213) 740-6709

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

#### Thursday, Jan. 22

NOON. "PTIP Associates with Histone Methyltransferase and Demethylase, and is Required for Adipogenesis," Kai Ge, NIDDK, NIH. HMR 100. Info: (323) 442-1144

#### Friday, Jan. 23

NOON. Hematology Grand Rounds. "ASH Updates on Multiple Myeloma," Sikander Ailawadhi, USC. IPT C2J103. Info: (323) 865-3950 **3 P.M.** Visions and Voices the USC Arts & Humanities Initiative. "Trust No One...or, How One Surgeon Actually Learned to Trust," Pauline Chen, USC. KAM Mayer Aud. Info: visionsandvoices@usc.edu

#### Tuesday, Jan. 27

**10** A.M. USC eco Supplier Expo. UPC: Town and Gown. Info: (213) 740-9791

11:30 A.M. Psychiatry Grand Rounds. "Benefits and Risks of Alcohol Use Among Older Persons," Alison Moore, UCLA. ZNI 112. Info: (323) 226-5572

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

**8:30** A.M. "Thyroid Storm," J. Lo Presti, USC. GNH 11-321. Info: (323) 226-7923

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

NOON. USC Center for Excellence in Teaching. "Emotional Intelligence," Win May, USC. KAM B21/23. Info: (213) 821-3925

**4 P.M.** Research Workshops 2009. "Developing and Submitting a NIH Grant Application," Steve Moldin, USC. UPC: CUB 329. Info: (213) 740-6709

#### Thursday, Jan. 29

**7 A.M. - 4 P.M.** "Accessing Government Funding for Research," Southern California Biomedical Council. UCLA. Info: (213) 236-4890

#### Friday, Jan. 30

**8** A.M. Pathology and Laboratory Medicine Grand Rounds. "Perspectives on Our Future in Pathology: The Journey Starts Today," Jared Schwartz, College of American Pathologists. NOR 7409. Info: (323) 442-1180

**11 A.M.** Hematology Grand Rounds. "ASH Updates on ITP," Howard Liebman, USC. IPT C2J103. Info: (323) 865-3950

NOON. Pharmacology and Pharmaceutical Sciences Seminar. "New Potential Therapeutic Targets for Diabetic Retinopathy," Edward Feener, Harvard. PSC 104. Info: (323) 442-1451

PLANS FOR THE FUTURE—Inderbir S. Gill (center), incoming chair of the Department of Urology, held an inaugural meeting for the USC Institute of Urology on January 8. Faculty, staff, residents and fellows gathered to hear Gill present his vision for the new institute.

### **Nanoscientist Joins School of Pharmacy**

Julio C. Camarero, one of three prolific young researchers recruited to the USC biomedical nanoscience initiative (see story on page 2), has joined the Department of Pharmacology and Pharmaceutical Sciences at the School of Pharmacy.

Camarero brings over a decade of experience in researching mechanisms of microbial disease and how these mechanisms relate to the immune system. His work aims to develop new technologies to find novel compounds that will block bacteria from causing disease.



Julio C. Camarero

Past work of the Spanish-born scientist has looked at anthrax and the Bubonic plague bacteria. He is also interested in the AIDS virus and hepatitis C.

"I am fascinated by pathogenesis – that is how microbes exploit and kill," says Camarero. "Pathogenic microbes are able to interface and modulate the host immune response to their own benefit, which ultimately results in disease. If we can inhibit or interfere with such molecular interactions, we should be able to disable pathogenic microbes without affecting the non-pathogenic ones."

At the Lawrence Livermore National Laboratory, Camarero was a Distinguished Lawrence Fellow before assuming the post of staff scientist.

### **HSC NEWSMAKERS**

speaker, location, and a phone number for information.

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

On Jan. 7, ABC News quoted fertility expert **Richard Paulson** about a pregnant woman who discovered she has two wombs.

A Jan. 8 *Orlando Sentinel* article quoted toxicology expert **Joseph Landolph** about investigation of a former military bombing range in Orlando, Fla., to see if it is causing cancer in area residents.

A Jan. 6 *Los Angeles Times* article quoted USC Norris oncologist **Heinz-Josef Lenz** about pancreatic cancer in a story about Apple Inc. CEO Steve Jobs' recent health issues.

A Jan. 4 *Washington Post* article highlighted work by **Songtao Shi** of the School of Dentistry in a widely carried story about tooth regeneration.

A Jan. 1 Washington Post article featured research by Parish Sedghizadeh of the School of Dentistry and colleagues which identified nine cases of osteonecrosis of the jaw among 208 patients taking oral antiosteoporosis drugs called bisphosphonates. The study was also featured by the Los Angeles Times, Daily Mail (U.K.), ABC News, Science News, Reuters Health, ABC News Boston affiliate WCVB-TV, ABC News Toledo, Ohio, affiliate WTVG-TV and All Headline News.

A Dec. 29 *Los Angeles Times* article quoted pharmacologist **James Adams** on the plausibility of a poisoning scenario in a recent episode of "The Mentalist."

A Dec. 29 McClatchy Newspapers article featured Doheny ophthalmologist **Mark Humayun** on retina implant advances.

A Dec. 24 United Press International article highlighted research by stem cell researcher **Qi-long Ying** and colleagues, reporting that the team has derived the first embryonic stem cells from rats. The research also was featured by Xinhua News Agency (China), *The Times* (UK), Science News and All Headline News. USC Health Sciences Public Relations 1975 Zonal Ave. KAM 400 Los Angeles, CA 90033 Non-Profit Organization U.S. POSTAGE PAID University of Southern California