MAY 4 • 2012

The Weekly

USC University of Southern California

theweekly.usc.edu

PUBLISHED FOR THE USC HEALTH SCIENCES CAMPUS COMMUNITY

VOLUME 18 • NUMBER 15

New, high-tech surgical suite debuts at Keck Hospital

By Alison Trinidad

A high-tech operating room that will help improve patient care debuted at Keck Hospital of USC on April 24, making it one of three Southern California hospitals with such a room, often called a "hybrid OR."

Cardiothoracic surgeon Vaughn Starnes and interventional cardiologist Ray Matthews led three back-to-back heart valve replacements on patients who are part of a U.S. clinical trial testing a non-surgical, minimally invasive treatment for aortic stenosis. To complete the experimental procedure, doctors need advanced imaging equipment to replace the diseased valve by threading a narrow catheter through the skin.

Typically, interventional procedures such as a transcatheter aortic valve implantation (TAVI) are performed in a catheterization lab, which is not equipped for surgery.

Imaging instruments are usually not found in ordinary operating rooms, since surgeons do not use cameras for open surgical procedures.

The new 1,100-square-foot hybrid room at Keck Hospital is designed for both catheter-based and surgical treatments.

"We would have done this procedure in the cath lab … but the real concern here is when things go bad," said Matthews, professor of clinical medicine and director of the interventional cardiology program at the Keck School of Medicine of USC. "We want to be in the best position to

See **HYBRID OR**, page 3

Photos/Alison Trinidad

Above, (from left) USC physicians David Shavelle, Vaughn Starnes and Ray Matthews perform an aortic valve replacement in a new hybrid operating room at Keck Hospital of USC. At right is the CoreValve—an experimental device being studied in a U.S. clinical trial to treat aortic stenosis, or narrowing of the aortic valve.

'This opens a whole new portal for us, in terms of the types of therapy we can provide to our patients.'

—Vaughn Starnes, chair of the Department of Surgery and surgeon-in-chief of the USC hospitals

USC research opens doors to better leukemia treatments

By Robin Heffler

Scientists in the Keck School of Medicine of USC have discovered that a protein commonly overexpressed in solid cancerous cells—one previously found to enable breast, prostate and other tumors to grow and resist treatment—is also overexpressed in multiple types of leukemia, and can be successfully targeted to block the disease.

"Our work further shows that if you suppress the level of the protein GRP78 in human leukemic cells, these cells are killed more efficiently by chemotherapy," said Amy Lee, professor of biochemistry and molecular biology at the Keck School and associate director for basic research at the USC Norris Comprehensive Cancer Center, who served as principal investigator of the study. "We discovered that GRP78 is necessary for the activation of the P13K/AKT signaling pathway, a major pathway that helps leukemia cells to survive, proliferate and become drug resistant."

The findings were recently published in the journal *Blood*. The research, which used mice models to study leukemia development and human leukemia cells to examine responsiveness to drug therapy, was funded by the National Cancer Institute.

Lee said that drug design is now under way to inactivate GRP78. "This novel approach to block the PI3K/AKT pathway could have great clinical implications for a wide range of cancers and may avoid complications that accompany other types of therapy," she said.

Joining Lee in the study, titled "Inducible knockout of GRP78/BiP in the hematopoietic system suppresses Pten-null leukemogenesis and AKT oncogenic signaling," were coauthors Shiuan Wey and Biquan Luo, graduate students in her lab; Chun-Chih Tzeng, a research assistant; and collaborators at New York University.

Violence Intervention Program moves to new center

By Ryan Ball

Operating in a tiny, dark and dingy room off of the emergency room at the Los Angeles County+USC Medical Center, Astrid Heger, a pediatrician specializing in child abuse, had her life changed by a seven-year-old girl who had been brutally raped on the train tracks in South Central Los Angeles. The girl came in draped in a dress made for a girl twice her age and the dirt from the assault was ground into her skin. Heger sent her assistant to a dollar store to buy underwear for the child and realized that there was a greater need beyond what she could do forensically.

"All I wanted to do was take her home and put her in my swimming pool. I wanted to give her a bath and clothes," Heger recalled decades later during the April 26 grand opening of the Violence Intervention Program Forensic Center and Community-Based Assessment and Treatment Center and Plaza, part of the LAC+USC Medical Center Outpatient Department.

As director of the Violence Intervention Program (VIP), Heger, a professor of clinical pediatrics at the Keck School of Medicine of USC, addressed a crowd assembled in the newly renovated 20,000-square-foot facility.

The space boasts an inviting lobby and waiting rooms, a childcare center, a high-risk premature infant clinic, a sexual assault center, a number of kid-friendly examination rooms, an area dedicated to adult protective services and an outdoor green space. Enlarged photos of staff members' children adorn the walls, and the airy

See **VIP**, page 3

Jon Nalick

Critical care nurse Rebecca Quintero (center) leads a tour of the new Violence Intervention Program's Assessment and Treatment Center, whose lobby is decorated with photos of the children of its staff members.

Stem cell therapy may keep immune system under control

By Beth Dunham

A new study, appearing in *Cell Stem Cell* and led by researchers at USC, outlines the specifics of how autoimmune disorders can be controlled by infusions of mesenchymal stem cells (MSC).

Highly versatile MSC originate from the mesoderm, or middle layer of tissue, in a developing embryo. MSC can be isolated from several kinds of human tissue, including bone marrow and the umbilical cord.

Principal investigator Songtao Shi, professor at the Ostrow School of Dentistry of USC's Center for Craniofacial Molecular Biology, said recent studies have shown the benefits of administering MSC to patients with immune-related disorders, such as graft versus host disease, systemic lupus erythematosus and rheumatoid arthritis.

These studies showed that infusions of MSC appeared to quell the production and function of overactive immune cells, including T- and B-lymphocytes. However, the specific mechanism behind how MSC get the immune cells under control hasn't been fully understood.

"MSC-Induced Immunoregulation Involves FAS-Ligand-/FAS-Mediated T Cell Apoptosis" examined how infused MSCs target and defeat overactive immune cells. Looking at the effects of MSC infusion in mice with systemic sclerosis (SS)-like immune disorders, Shi and his colleagues discovered that a specific cellular mechanism known as the FAS/FAS-ligand pathway was the key to the remarkable immune system benefits.

Specifically, in mice with SS-like disorders, infusions of MSC caused T-lymphocyte death with FASL/FAS signaling and lessened symptoms of the immune disorder. However, MSC deficient in FAS-ligand failed to treat immune disorders in SS-afflicted mice.

With the hopeful results of the animal model study in mind, Shi's colleagues in China performed a pilot study with patients suffering from SS. Infusions of MSC provided similar clinical benefits to patients, and experimental analysis revealed that the FASL/FAS pathway also was at work in humans with SS.

The identification of the cellular workings responsible for the success of the stem cell treatments eventually may help doctors find optimal cell-based treatment for some immune diseases, Shi said.

The National Institute of Dental and Craniofacial Research and the California Institute for Regenerative Medicine supported basic research portions of the study. Clinical studies were supported by a grant from the China Major International (Regional) Joint Research Project.

USC researcher awarded grant for human genome research

Peggy Farnham, professor of biochemistry and microbiology at the Keck School of Medicine of USC, was awarded one of 10 National Human Genome Research Institute (NHGRI) grants intended to develop groundbreaking technologies that may one day shed light on the secrets of the human genome.

Farnham, who has been part of the NHGRI Encyclopedia of DNA Elements (ENCODE) project for the past eight years, will receive $540,000 over two years to test the function of genomic regions that bind large numbers of regulatory proteins.

Farnham's team will precisely remove parts of the genome and ask how neighboring genes are affected.

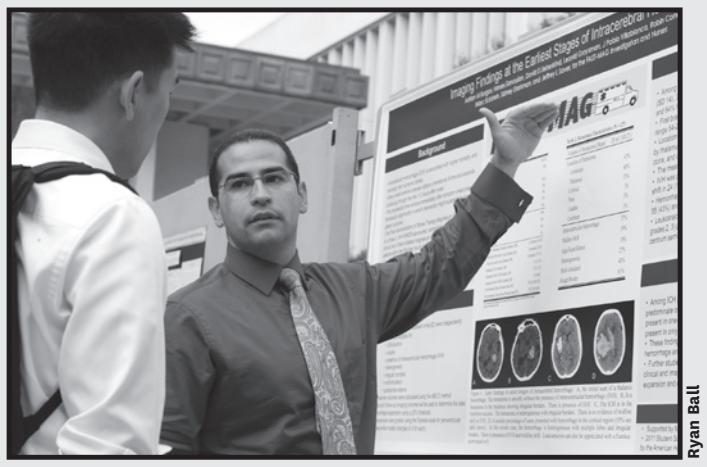
Peggy Farnham

The 10 grants total $10.5 million and were awarded to researchers at the Massachusetts Institute of Technology (MIT), University of Michigan, University of Washington School of Medicine, University of Washington, Washington University in St. Louis, University of North Carolina at Chapel Hill, Broad Institute of MIT and Harvard, Memorial Sloan-Kettering Cancer Center, and Dana-Farber Cancer Institute.

The ENCODE project was established to determine how the sequence of the human genome communicates to our bodies at a molecular level. The NHGRI is part of the National Institutes of Health.

In 2011, Farnham was part of a team that developed "A User's Guide to the Encyclopedia of DNA Elements (ENCODE)," published in *PLoS Biology*, providing a guide for using the vast amounts of data and resources produced by the project.

Farnham is holder of the William M. Keck Endowed Chair in Biochemistry at the USC Norris Comprehensive Cancer Center.



Ryan Ball

POSTER DAY—*Keck School student Adrian Burgos, presents his findings as part of Medical Student Research Forum and Poster Day on April 30. The annual event provides medical students with the opportunity to present their basic science and clinical research to their peers and the USC community at large.*

2012 Commencement Ceremonies

Wednesday, May 9

Keck School of Medicine – M.S., Ph.D., & M.P.H.

4 p.m. at the Norris Library Quad on the Health Sciences campus. Keynote speaker: Irving Weissman, director of the Institute of Stem Cell Biology and Regenerative Medicine at Stanford University. A reception will immediately follow at the same location. No tickets required. More Info: 323-442-1607

Friday, May 11

Occupational Science and Occupational Therapy

10:45 a.m. at the lawn west of Leavey Library at the University Park campus. Keynote speaker: Ronnie Chan, USC trustee and chairman of Hang Lung Group Limited and Hang Lung Properties Limited. A reception will immediately follow at the Davidson Conference Center, Embassy Room. No tickets required. More Info: 323-442-2811

Physician Assistant Program

10:45 a.m. at the lawn southwest of the Allan Hancock Foundation Building at the University Park campus. Keynote speaker: James Delany, president of the American Academy of Physician Assistants and USC Physician Assistant Program alumnus, class of 1975. A reception will immediately follow at the same location. No tickets required. More Info: 626-457-4253

Biokinesiology and Physical Therapy

11 a.m. at Bovard Auditorium at the University Park campus. Keynote speaker: Bill Shumard, president and CEO of Special Olympics Southern California. A reception will follow at 12:30 p.m. at the Davidson Conference Center. No tickets required. More Info: 323-442-5550

Dentistry

11 a.m. at McAlister Soccer Field at the University Park campus. Keynote speaker: John Robinson, former USC football coach. A reception will follow at 1:30 p.m. at the same location. No tickets required. More Info: 213-740-2851

Health Promotion

11 a.m. at Town and Gown at the University Park campus. Keynote speaker: Elahe Nezami, director of the Health Promotion and Disease Prevention Studies Program and the Global Health Program at the USC Institute for Health Promotion and Disease Prevention Research. A reception will be held at 10:30 a.m. at the same location. Tickets are required for the ceremony, but not for the reception. More Info: 213-821-1601

School of Pharmacy

3 p.m. at the Norris Library Quad on the Health Sciences campus. Keynote speaker: Virginia Herold, executive officer of the California Board of Pharmacy. A reception will immediately follow on the Upper Quad. Tickets are required. More Info: 323-442-1383

Saturday, May 12

Keck School of Medicine – M.D./Ph.D., M.D.

3 p.m. at the Shrine Auditorium in Los Angeles. Keynote speaker: Nadine Gracia, acting deputy assistant secretary for minority health and acting director of the office of minority health at the U.S. Department of Health and Human Services. A reception will immediately follow on the McCarthy Quad at the University Park campus. No tickets are required. More Info: 323-442-2553

The Weekly

Next Issue: May 11

The Weekly is published for the faculty, staff, students, volunteers and visitors in the University of Southern California's Health Sciences campus community. It is written and produced by the Health Sciences Public Relations and Marketing staff. Comments, suggestions and story ideas are welcome. Permission to reprint articles with attribution is freely given.

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USC researchers uncover a protein's role in genetic repair, stability

By Robin Heffler

Examining basic cellular processes, researchers at the University of Southern California have discovered how an anti-tumor protein plays an important role in activating the process of repairing damaged DNA, and a direct role in maintaining chromosomal stability. With chromosomal chaos long being linked to cancer, the findings are expected to help researchers eventually develop cancer-fighting tools.

Chengyu Liang, an assistant professor of molecular microbiology and immunology at the Keck School of Medicine of USC, is the corresponding author for a paper titled "A dual role for UVRAG in maintaining chromosomal stability independent of autophagy," published online April 26 in the journal *Developmental Cell*. Also contributing significantly to the research were first author Zhen Zhao, a USC postdoctoral fellow in Liang's laboratory, and Soohwan Oh, a former technician in the lab and currently a doctoral student at UC San Diego.

The research unveiled a new role for the protein UV irradiation resistance associated gene (UVRAG), which is at work during the routine cellular self-cleaning and recycling process called autophagy.

"Basically, UVRAG acts as a scaffold or adaptor protein by binding to and activating the DNA-dependent protein kinase (DNA-PK) enzyme," Liang said. "When there is a double-strand break, one of the most severe types of DNA damage, DNA-PK fixes the damage through a kind of gluing process."

Conversely, Liang said, when UVRAG is removed from the cells, DNA-PK activity is impaired or reduced. "As a result, the cells can't repair damaged DNA in a timely and accurate manner, and this damage accumulates in cells, which results in structural alterations of the chromosomes and enables tumors to grow."

Previously, Liang and her co-investigators had identified UVRAG as a tumor suppressor that activates the autophagy pathway in cells. They had found that UVRAG plays a critical role in both early and late stages of autophagy, which rids cells of toxins, viruses and bacteria.

With the latest study, which was funded by grants from the National Institutes of Health, the American Cancer Society and the Baxter Foundation, the researchers also discovered that UVRAG helps to stabilize the number of centrosomes, specialized structures in the cell that play an important role in cell division.

"We found that UVRAG helps to maintain the correct number of centrosomes, and that if it is deleted or reduced, the centrosomes multiply and duplication during cell division becomes out of control," Liang said. "As a result, the genetic material can't equally divide into daughter cells, and the number of chromosomes will change to either too many or too few."

When that happens, it causes problems with growth, development and functions of the cell's system.

"UVRAG seems to be new cells' guardians," she added, "keeping an eye on our DNA and centrosomes, fixing damage and preventing improper cell division. So this study represents a major conceptual advance in understanding UVRAG's role as an autophagy-related protein in the suppression of cancer, while at the same time unfolding elegant mechanisms whereby UVRAG acts to maintain genomic integrity."

Liang said that future research will focus on an in-depth analysis of how UVRAG maintains the integrity of centrosomes, how UVRAG's dual roles during DNA damage repair and cell division are coordinated and how UVRAG's role in autophagy is related to these dual roles.

'UVRAG seems to be new cells' guardians ... fixing damage and preventing improper cell division.'

—Chengyu Liang, an assistant professor of molecular microbiology and immunology at the Keck School of Medicine of USC

VIP: Hundreds celebrate center's grand opening

Continued from Page 1

lobby also serves as a gallery for area artists.

"We may be in East L.A. and we may be taking care of people who are poor, who are underprivileged or minorities who may not speak English, but they deserve to walk into a place that looks every bit as good as the clinic I walk into when I go to a doctor in Pasadena," said Heger. "They deserve to have a place where they feel safe."

Made possible by a groundswell of support from foundations and private donors, the facility is a monument to Heger's dedication to patient welfare and her dogged determination.

"It always amuses me to do the things that people say they don't think I can do," Heger said with a sly grin. "I find it highly entertaining."

For more information and to become a member of the VIP volunteer membership circle, visit violenceinterventionprogram.org.

Jon Nalick

Astrid Heger (left), professor of clinical pediatrics at the Keck School of Medicine of USC, visits with Linda (center right) and Tony Rubin (right) and their daughter Gena at the center's grand opening. The Rubins' gift help fund the center.

HYBRID OR: New room boosts medical capabilities

Continued from Page 1

take care of the patient, and in an operating room like this we can instantly convert to an open surgical procedure without moving the patient [from the lab to the OR]. It's a much safer situation for the patient."

The hybrid room is equipped with multiple high-definition cameras and video monitors that give surgeons better views of the operating field during minimally invasive surgery. Using technology developed by Karl Storz Endoscopy-America, the audiovisual system links with electronic lab records and hospital information systems and can support live, on-demand teleconferencing.

The system allows surgeons to use a laptop device to access live and stored surgical video files through an Internet link, watch live cases as they are being performed, and communicate between ORs.

"This combines the operating room and catheterization laboratory into one, giving us the capability to perform procedures like coronary or aortic graft stenting and open heart surgery at one time," said Starnes, chair of the Department of Surgery and surgeon-in-chief of the USC hospitals. "This opens a whole new portal for us, in terms of the types of therapy we can provide to our patients."

Mark Cunningham, assistant professor of cardiothoracic surgery at the Keck School, spearheaded the design of the hybrid suite at Keck Hospital, visiting hospitals across the country for the best technology available. Although the room is targeted to augment cardiovascular therapies, Cunningham said the setup will also benefit general surgery and other specialties such as neurological and laparoscopic services.

To view video of the hybrid OR, visit http://keck.usc.edu/hybridOR.

Use your smart phone to scan the QR code at left to view video of the new hybrid OR.

The Weekly NEWSMAKERS

The May 2 edition of ***Modern Medicine*** quoted **Neda Shamie**, associate professor of clinical ophthalmology at the Keck School, about a modified surgical technique that facilitates optical graft preparation.

An April 30 broadcast of MSNBC's "Morning Joe" featured an interview with **David Agus**, professor of medicine at the Keck School, about his book ***The End of Illness***.

An April 29 report in ***The Chronicle of Higher Education*** noted that stem cell scholar **Andrew McMahon** will leave Harvard University to direct the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC, housed within the Keck School. McMahon will chair the university's new Department of Stem Cell Biology and Regenerative Medicine. Most of the team from McMahon's Harvard laboratory will come with him to USC, and he will also be hiring roughly 12 scientists for new positions.

An April 26 article in the ***Los Angeles Times*** quoted **Astrid Heger**, professor of clinical pediatrics at the Keck School, about the opening of a newly renovated building for the Violence Intervention Program at LAC+USC Medical Center. Heger is director of the program, which treats victims of violence and abuse.

An April 25 story in ***Medscape Medical News*** quoted **Helena Chui**, chair of the Keck School's neurology department and director of USC's Memory and Aging Center, about how PET scan readings may lead to misdiagnosis of Alzheimer's disease. "Actually, when I do the full work-up, I sometimes tell these patients, the good news is that I don't think you have Alzheimer's disease," Chui noted. "Then I look at the PET scan and I also don't think the PET scan supported AD."

An April 25 post on Business Insider quotes a blog that cites a review paper co-authored by the Keck School's **Steven Sussman**, professor of preventive medicine, and doctoral student **Nadra Lisha** about 11 potentially addictive behaviors, including love.

An April 24 story on Kaiser Health News about Los Angeles County's health services director quoted **Michael Cousineau**, associate professor of family medicine and preventive medicine at the Keck School.

An April 24 article in the ***Daily Mail*** (U.K.) quoted **William "Billy" Mallon**, associate professor of clinical emergency medicine at the Keck School, about teenagers distilling hand sanitizer to get drunk. Mallon also was interviewed by CW News Los Angeles affiliate KTLA-TV.

Calendar of Events

This Calendar of Events is also online at www.usc.edu/hsccalendar for the Health Sciences campus community

Wednesday, May 9

9 a.m. - 4 p.m. USC AirPollBrain Retreat 2012. Various speakers. ZNI 112. Info: (323) 442-2144

Saturday, May 12

7 a.m. - noon. Revlon Run/Walk For Women at Los Angeles Memorial Coliseum at Exposition Park. The cost to run/walk is $35 through May 11 ($40 day of the event). Your registration fee includes an EIF REVLON Run/Walk For Women T-shirt and goodie bag. It will also include a USC Norris Team T-shirt. Info: (323) 865-0668

Monday, May 14

Noon. KSOM Research Seminar. "KSHV: Latency and Reactivation," Blossom Damania, University of North Carolina - Chapel Hill. NRT Aresty Aud. Info: (323) 442-7732

Tuesday, May 15

10 a.m. Keck Medical Center of USC Guild Outreach Speaker Series. "Regenerative Medicine: An Organ Recital," David Warburton, USC/CHLA. Presentation of Outstanding Faculty Award to Henri Ford, USC/CHLA. Private Club in Pasadena. Reservations by May 7 and Info: (626) 440-0679

Wednesday, May 16

Noon. ZNI Seminar. "Mitochondrial Dynamics in Mammals," David Chan, CalTech. ZNI 112. Info: (323) 442-2144

Friday, May 18

8:30 a.m. Surgical Grand Rounds: Clinical Research Presentations from Breast/Soft Tissue and Endocrine Surgery. DOH 1st Floor Auditorium. Info: (323) 442-2506

10 a.m. - 3 p.m. HTE @ USC Second Annual Frontiers Symposium. "Matchgame 2012: Linking Clinical Needs with Engineering Know-how," Dave Marvit, Fujitsu Laboratories of America. SSB 1st Floor Conference Room. Info: (323) 442-7732

Monday, May 21

1 p.m. - 4:30 p.m. ZNI Mini-Symposium. "Advancing Biomedical Technologies," various speakers. ZNI 112. Info: (323) 442-2144

Friday, May 25

8:30 a.m. Surgical Grand Rounds. "Instrumental: A Tale of the Tools of Our Trade Told in Verse," Jonathan Hiatt, UCLA. DOH 1st Floor Auditorium. Info: (323) 442-2506

Thursday, May 31

Noon. Cardiology Grand Rounds. "Diabetes and Stable Ischemic Heart Disease," Prakash Deedwania, UCSF. BCC 1st Floor Conference Room. Info: (323) 442-7419

Friday, June 8

8 a.m. - 5 p.m. Stem Cell Research at USC Stem Cell Symposium. "The Stem Cell Niche in Development and Regeneration," various speakers. NRT Aresty Aud. Info: (323) 442-8080

Friday, June 15

8:30 a.m. - 2 p.m. Southern California Alzheimer's Disease Centers Research Symposium 2012. "Vascular Cognitive Impairment and Dementia," various speakers. UPC: GER Auditorium. Info: (323) 930-6280

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 *The Weekly*, KAM 400 or fax to (323) 442-2832, or email 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.

Susan Autry (in red), executive director of USC's Southern California Clinical and Translational Science Institute, joins colleagues from the U.S. and China in Shanghai as part of a series of workshops designed to help teach the Chinese how to build clinical and translational research institutes (CTSIs) and centers.

USC research institute trains academic leaders in China

By Nasim M. Thompson

Susan Autry, executive director of USC's Southern California Clinical and Translational Science Institute (SC CTSI) recently joined a distinguished roster of academic leaders from Shanghai Jiao Tong University and the Chinese Academy of Medical Sciences in Shanghai, China, to conduct a series of training workshops on how to build clinical and translational research institutes (CTSIs) and centers.

The three-day workshop, held March 23-25, explained the history and concepts of clinical and translational research at academic health centers in the U.S. and other countries; taught effective ways to build leadership teams at CTSIs; and taught how to develop the key components of CTSIs, such as training programs, clinical research support, informatics and collaborations with industry.

Tom Buchanan, director of the SC CTSI, said, "Susan's visit to China is an exciting first step in bringing the SC CTSI's experience in clinical and translational research to the global stage. We intend to continue positioning ourselves as both national and global leaders in clinical and translational research."

Distinguished leaders at the workshop included Barbara Alving, former director of the NIH National Center for Research Resources—the NIH center that developed the Clinical and Translational Science Awards (CTSA) program, which funded the SC CTSI; Michael Conlon, associate director and chief operating officer at University of Florida's CTSI; Paul Harris, associate professor of biomedical informatics and director of the Office of Research Informatics at Vanderbilt University; and Tesheia Johnson, chief operating officer of the Yale Center for Clinical Investigation.

Attendees—executives and administrators from major hospitals and universities working to establish clinical and translational centers in China—included representatives from Shanghai Jiao Tong University School of Medicine, Nanjing Medical University, Chinese University of Hong Kong and the Shanghai Food and Drug Administration.

The SC CTSI is one of 60 premier research institutes in a national consortium that aims to speed the translation of research discoveries into solutions for better health.

ONLINE EXTRAS

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  http://tinyurl.com/ctcqth9

- **Karen Bass luncheon kicks off student advocacy trip**
  http://tinyurl.com/75yukqd

- **Occupational Therapy "Lights It Up Blue" for World Autism Awareness Day**
  http://tinyurl.com/76qd6wc

- **Keck School scientist finds higher risk for ovarian cancer for women with endometriosis**
  http://tinyurl.com/6wz7hxm

- **Turkish urologists visit USC Institute of Urology**
  http://tinyurl.com/75sxcoq

- **Going for the gold at World Health Day L.A.**
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