Welcome to the Summer Issue of the Keck Research Quarterly. The regular faculty spotlight features Neil Kaplowitz, MD, who has been a leader in liver disease research at USC since 1990. Our regular feature on research programs and resources features two NIH-funded centers, the USC Research Center for Liver Diseases, directed by Neil, and the Southern California Research Center for Alcoholic Liver and Pancreatic Diseases (ALPD), directed by Hidekazu Tsukamoto, DVM, PhD. In the Research Dean’s Corner, I introduce two new associate deans who will be working with me to advance the Keck School’s research agenda in areas of clinical research (April Armstrong) and basic and translational research (Sarah Hamm-Alvarez). This issue also contains updates on faculty honors and promotions, as well as new information from Janet Stoeckert on resources for grants management. I hope you enjoy reading this summer issue of the Keck Research Quarterly.

Tom Buchanan, MD
Vice Dean for Research

Faculty Spotlight

Neil Kaplowitz, MD
BS, MD, New York University

Dr. Neil Kaplowitz is the USC Associates-Brem Professor of Medicine, Garrie-Budnick Chair in Liver Disease and chief, division of gastrointestinal and liver disease in the Department of Medicine. He is also the director of the NIDDK-sponsored USC Research Center for Liver Disease. His major research focus is in liver diseases and the effects of drugs and alcohol on the liver. His laboratory studies the convergence of signal transduction, mitochondrial dysfunction, oxidative stress, ER stress and cell death pathways in the pathogenesis of liver injury in cell and animal models.

What initially attracted you to liver function and liver diseases?

As I developed an interest during medical school in the regulation of biochemical and physiological processes in the liver (see below), I naturally wanted to link this research with human illness, particularly what I was seeing in the hospital — both initially as a trainee and later as a faculty member. Physician-scientists have a unique perspective in having a deep appreciation of clinical relevance and important issues that we face in diagnosis and treatment. Although my research focus has been largely laboratory-based, the hospital work and bedside teaching has always kept my laboratory research goals focused on clinical relevance. So my specialization in hepatology has evolved simultaneously with my research interests.

As a clinician, what attracted you to research?

Career paths are heavily influenced by great teachers who present complex information in a lucid fashion, providing insight. For me, as a medical student, there were two: Severo Ochoa, a physician-scientist and Nobel laureate who taught biochemistry by explaining the experimental approaches to the great discoveries of the time (e.g., Kreb’s cycle and genetic code), and Norman Javitt, also a physician-scientist. He taught about metabolism and transport of bilirubin and bile acids, as well as the physiological basis of bile secretion and the mechanisms of cholestatic jaundice. This introduction, along with the challenge of diagnosis and treatment of an organ not readily accessible to direct examination and a rich center of unexplored biochemistry and physiology, fascinated me. If I had had similar experiences with neuroscientists, cardiologists or nephrologists, who knows what would have happened. After Norman Javitt’s lectures in year 2 of medical school, I asked him if I could do research with him. He suggested that I might work on porphyria, a group of genetic metabolic diseases that

Continued on page 2
manifest due to defects in the pathway to heme synthesis. Norman and a dermatology collaborator were seeing a number of cases of photosensitive protoporphyria and this was not an area Norman had investigated. So, I went to the library and read everything I could and came back to him with an idea that lead to a year of research during medical school and a publication in the New England Journal of Medicine. From there, I just built on the logical progression from porphyrins (pyrroles) to heme (cytochrome P450s and drug metabolism) to its breakdown to bilirubin. I later worked again with Norman during a GI fellowship. Again, he made another important suggestion, namely that I determine if the liver cytoplasmic proteins that bind bilirubin also bind bile acids. I set out to do this, but was quickly diverted by the discovery that the binding proteins were glutathione (GSH) S-transferases, which are enzymes of detoxification. This led me into the field of toxicology and drug toxicity, initially studying the biochemistry and regulation of these enzymes and GSH itself. Ultimately, one thing builds on another, as I became more and more focused on oxidative and organelle-derived stress responses, signal transduction, and mitochondrial dysfunction in the pathogenesis of cell death in animal models of liver disease. Norman placed the seed and I went with it wherever it would logically take me. I try to do the same for my mentees.

What other areas of research have you collaborated and how have these collaborations advanced or influenced your own research?

I have had a longstanding collaboration with the Fernandez-Checa lab in Barcelona, since he moved from my lab at USC in 1993. We share common interests in the dysregulation of mitochondrial GSH and the role of ER stress in the pathogenesis of alcoholic liver disease. This has been mutually beneficial, advanced our independent work and provided novel insights that extend beyond alcoholic liver disease. We work together at USC every summer, supported by one of the funded projects of the Southern California Research Center for ALPD grant based at the Keck School.

Over the years, I have frequently found interesting challenges, and tried to develop new insights in my areas of clinical interest — drug-induced and alcoholic disease — through collaborations at the Keck School with colleagues such as the late Telfer Reynolds, and Andrew Stolz, as well as outside the Keck School with the drug-induced injury clinical research group of Andrade and Lucena in Malaga, Spain, and NIDDK Drug-Induced Liver Injury Network and an NIAAA-sponsored Southern California Alcoholic Hepatitis Network. In addition, as consultant for pharmaceutical companies, I have mainly assisted in identifying and understanding the mechanism of hepatotoxicity of drugs in both preclinical and clinical development. All of these clinical collaborations have led to publications and provide new insights, which I have taken under consideration in advancing my own laboratory research. In one case in particular, the initial consultations on antisense molecules developed by ISIS Pharmaceuticals directed at potential therapeutic targets in liver disease have led to a decade-long collaboration, which has greatly advanced my research on the role of signal transduction and cell death pathways in the pathogenesis of liver injury in animal models. The key is that my curiosity is aroused in any context, including the clinical setting, and I enjoy trying to learn something new.

What do you think will be the next big advance in your field, and what do you think the Keck School can do to position itself to be a leader in this area?

Two of the most common liver diseases, hepatitis B and C, will be diminishing due to the great advances in therapy. The remaining common causes of cirrhosis are fatty liver disease (linked to obesity and diabetes) and alcoholic liver disease. We have great strength in basic and clinical research in alcoholic liver disease, but lag in fatty liver disease. Although we have considerable strengths in diabetes and obesity at USC, we need to strengthen both our basic science research in lipid metabolism and our clinical research in the hepatological aspects of this major disease through several key recruitments. Ultimately, a multidisciplinary approach with visionary leadership of a senior clinician-scientist in this field would position us to play a major role. We need a well-supported registry of patients, lipidomics, biobanking and clinical trials on biomarkers of progression and treatment.

Liver immunology is a key area that needs to be developed. We are learning that the regulation of the adaptive immune system plays a role in the pathogenesis of viral, autoimmune, transplant rejection and drug-induced liver disease. Dysregulation of immune tolerance, specifically in the liver, may explain a great deal about the pathogenesis of idiosyncratic drug-induced liver disease — a major cause of acute liver failure and failure of drugs in development and post marketing. We have a great deal of strength in innate immunity, but to face
the challenges of immune-mediated liver disease, a key recruitment of an established investigator in liver-specific adaptive immunity and its translational applications would be critical to position USC to advance this field.

Other important emerging areas include prevention and individualized treatment of liver cancer and the prevention or reversal of fibrosis and cirrhosis. We have outstanding investigators at the forefront of these areas. Major advances in stem cell and regenerative medicine are likely to occur over the next decade, which will provide rescue of acute liver failure and repair of cirrhosis. The Eli and Edythe Broad CIRM Center for Regenerative Medicine and Stem Cell Research at USC provides an exceptional base for advancing this field. However, an established scientist who can lead a basic and translational liver program is missing and would be critical for us to be in the forefront of the applications of this promising field to liver disease.

We have a wonderful mix of basic science and clinical research in liver disease at USC, arguably among the best in the nation. However, several key recruitments — along with appropriate resources — would strategically position us to leap ahead and be at the forefront of the emerging areas likely to lead to new advances in the prevention and treatment of liver disease.

What advice would you give to junior faculty about being competitive in receiving grant funding?

First, one needs to be in a supportive environment that provides strong, dedicated mentorship, protection of time for research, and access to routine and cutting edge technologies through center and institutional core facilities. Second and even more importantly, the science needs to be strong with respect to its importance or novelty, the availability of convincing preliminary data, and some published track record that attests to the feasibility of the proposed work. Third, it is critical to remain focused and not over extend. Thus, one has to place his or her work in context, convince the reviewers that it is important to conduct the work and that it will significantly advance the field, that he or she has the capability of completing what is proposed (based on preliminary data and collaborative resources available), and that it will dig deep in one place rather than scratching the surface in multiple places. Ultimately, the quality of the science and novelty will prevail.

The NIH's new Genomic Data Sharing Policy, issued on August 27, 2014, has gone into effect, beginning with grant applications submitted for the January 25, 2015 due date. Applicants are expected to state in the cover letter when a proposed study will generate large-scale human and/or nonhuman genomic data, and include a genomic data sharing plan in the application, according to a reminder notice issued December 4, 2014 (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-027.html). If sharing of human data is not possible, applicants should provide a justification explaining why data sharing is not possible and provide an alternative data-sharing plan.

If you are looking for help with your budget or assembling grant sections, Janet Stoeckert, Director of Research Advancement, is available to assist you. Contact Janet at (323) 442-3568 or email janet.stoeckert@usc.edu.
This system is located in the Center for Electron Microscopy and Microanalysis (CEMMA) at the University Park Campus, a 20-minute shuttle ride for Health Sciences Campus users. John Curulli leads the core. The system includes an optical-sectioning epifluorescence microscope, a 20x objective, and a high-magnification objective. The microscope is equipped with a Hamamatsu ORCA-R2 digital camera and a high-speed, 12-bit, cooled charge-coupled device (CCD) camera. The microscope is also equipped with a water-cooled objective turret and a full set of accessories, including a motorized stage, a manipulator, and a high-quality light source. The microscope is capable of high-resolution imaging and analysis of samples using a wide range of fluorescent and transmission electron microscopy techniques. In addition, the core provides technical support and training for users, as well as access to a wide range of advanced microscopy and image analysis software.

For the most part, access to the cores is restricted to Center members and the procedure for application for membership can be found at the website. Members must be working in the field of liver disease. In some cases, access of non-members to cores is available with lower priority.

The four scientific cores provide technical staff and equipment necessary to support the needs of Center members.

1) Cell Separation and Culture Core (Director, Bangyan Stiles, Associate Director, Zhang-Xu Liu): This core has been expanded from a longstanding central core that has been a workhorse, preparing primary hepatocyte cultures from normal and diseased mice and rats and various cell lines to a wide range of investigators — by the addition of a Cell Separation sub-core, with instrumentation and expert leadership of a liver immunologist (Dr. Liu) to perform FACS analysis and magnetic cell separation/isolation. The new sub-core also provides core services, and Seahorse XC Flux Analyzer metabolomics. The core also provides technical support and training for users.

2) Liver Histology Core (Director, Gary Kanel): This core provides a wide range of standard and customized slide preparation, histochemistry and immunohistochemistry of liver samples obtained from animals, as well as laser-capture microscopy under the direction of an outstanding liver pathologist, Dr. Kanel. Dr. Kanel also provides expert consultation in interpretation of findings, collaborations, and technical oversight.

3) Analytic, Metabolic, and Instrumentation Core (Director, Murad Ookhtens): This core maintains and provides access and training in the use of major and expensive equipment items, including thermocyclers, plate readers, centrifuges, standard and customized HPLC services, and Seahorse XC Flux Analyzer metabolic applications. Samples for HPLC are brought to the core and run by the technical staff. The core also provides training in the use of equipment. The full list of equipment, location and procedure for access can be found on the website. Dr. Zandi is associate director of the core and directs the state-of-the-art Proteomic Sub-Core. The Proteomic Sub-Core is available to the entire University and is partially supported by the Liver Center in exchange for priority access and discounted services.

4) Cell & Tissue Imaging Core (Director, Sarah Hamm-Alvarez): This core provides support for confocal and fluorescence microscopy, including access, consultation, technical support and training. The core has a Zeiss LSM 510 microscopy system and a Nikon Diaphot fluorescence microscope. Both are older instruments, but are maintained by the core and are highly suitable for routine applications. The core provides direct technical support and training for Liver Center members and their laboratory staff in identifying and processing images of interest. Experienced users can operate the equipment independently. In order to expand the capabilities of the core and provide Liver Center members with advanced technologies, beginning in Dec. 2015, the core will offer seminars describing the latest imaging advances and support access to other technologies in the University. Liver Center members will be able to apply for up to $2,500 pilot grants to defray the costs of using other university microscopy cores. Applications will be reviewed by an internal advisory committee. The instruments that will be available through this initiative include:


- This system is located in the Center for Electron Microscopy and Microanalysis (CEMMA) at the University Park Campus, a 20-minute shuttle ride for Health Sciences Campus users. John Curulli leads the core. The system includes an optical-sectioning epifluorescence microscope developed by the University of California, Los Angeles (UCLA). The microscope is equipped with a Hamamatsu ORCA-R2 digital camera and a high-speed, 12-bit, cooled CCD camera. The microscope is also equipped with a water-cooled objective turret and a full set of accessories, including a motorized stage, a manipulator, and a high-quality light source. The microscope is capable of high-resolution imaging and analysis of samples using a wide range of fluorescent and transmission electron microscopy techniques. In addition, the core provides technical support and training for users, as well as access to a wide range of advanced microscopy and image analysis software.
THE SOUTHERN CALIFORNIA RESEARCH CENTER
FOR ALCOHOLIC LIVER AND PANCREATIC DISEASES

Alcoholic liver and pancreatic diseases (ALPD) and cirrhosis constitute leading lifestyle diseases around the globe. The Southern California Research Center for ALPD and Cirrhosis unifies 57 investigators from major academic institutions in Southern California to pursue a common mission of being a leader in research, training and outreach for the diseases. The center, since its inception in 1999, has devoted its efforts for development and use of clinically relevant animal models to gain novel insights into the molecular mechanisms underlying the predisposition to advanced ALPD. These efforts culminated in recent groundbreaking discoveries, which have significantly advanced the understanding of synergistic ALPD caused by alcohol and second or multiple hits. In the past five years the center’s interactive environment and infrastructure have facilitated a 152 percent increase in research base to $8.5 million/year; four new U01/ P01 programs; 198 publications; generation of 14 NIH-funded early-stage investigators; transition of eight postdocs to faculty positions; training 166 graduate and 20 undergraduate students; and organizing three community seminars and four international symposia. As an unique national resource, the center has provided to scientific communities across the nation:

- 229 rodents as ALPD models and 204 model samples for 17 outside investigators;
- 329 liver cell isolation preparations for 14 investigators; and
- Support for grant acquisition and application by 12 outside investigators since the last renewal.

The center is a unique scientific center of excellence in ALPD and cirrhosis promoting:

1) An environment conducive to leading-edge research on the center’s main theme: elucidation of the priming and sensitizing mechanisms for ALPD;

2) Provision of unique models, innovative genetic approaches and expertise to outside investigators, including those at other NIAAA Alcohol Research Centers;

3) Comprehensive education and research training at multiple levels, ranging from undergraduate and graduate students, postdocs to junior faculty, to foster future generations of scientists in ALPD and cirrhosis; and

4) Outreach efforts to disseminate the center’s new findings to lay public.

The center supports three research cores:

**Animal Core** - This core focuses on research on in vivo genetic analysis and synergism between alcohol and risk factors for the pathogenesis of alcoholic liver and pancreatic diseases (ALPD) by investigators within and outside of the center. The core has developed a new mouse hybrid model of ad lib feeding of Western diet and iG ethanol infusion, which produces alcoholic liver fibrosis and the hybrid plus binge model, which — for the first time — reproduces histological evidence of alcoholic hepatitis. Alcohol-fed HCV NS5A/Core transgenic (tg) models produce liver tumor and are successfully utilized for isolation and characterization of tumor-initiating cells. Using knockout, knock-in, and Tg mice, these models allow invaluable genetic deletion and addition analysis, providing researchers the unique opportunity to test the importance of a single gene of interest in the genesis and evolution of ALPD. The core also incorporates chimeric and genetic mice into the iG models to test the role of bone marrow-derived cells and to enable genetic tracing of Kupffer cells and myofibroblasts in the pathogenesis of alcoholic liver injury and fibrosis. The core currently has the capacity to produce ~750 rodent models per year, of which 65 percent are served as the iG model. In the past 5 years, the core has conducted 167 experiments with 2,499 rodents for 32 center and nine non-center scientists; and contributed to 51 publications and 26 NIH/VA grants newly acquired or competitively renewed by these investigators. The core also facilitated 28 collaborative projects via the shared use of animals and tissues, and application of complementary scientific expertise to the models. With the innovative models and techniques, the core strives to serve the ALPD scientific community as a unique and invaluable national resource. For related references, link to: http://keck.usc.edu/en/Research/Centers_and_Programs/Research_Center_For_Alcoholic_Liver_and_Pancreatic_Disease/Core/Animal_Core.aspx

**Integrative Liver Cell Core** Integrative Liver Cell Core - The Non-Parenchymal Liver Cell Core, now re-named to “Integrative Liver Cell Core” (ILCC), strives to serve the scientific community of alcoholic liver disease (ALD) and cirrhosis via specialized services of isolation of 6 different liver cell types (hepatocytes, HC; hepatic macrophages, HM; hepatic stellate cells, HSC; liver sinusoidal endothelial cells, LSEC; liver mesothelial cells, MC; and CD133+ liver progenitor cells) from normal rodents and rodent models of ALD and liver fibrosis. The most powerful outcome ensues when these services are applied to the rodent models of ALD or liver fibrosis, allowing direct analysis of specific cellular changes in the evolution of the diseases. This approach is achieved by the ILCC’s close collaboration with the Animal Core of the NIAAA-funded Southern California Research Center for ALPD and Cirrhosis and allows isolation of the different cell types from diverse pathologic spectra. These models include the intragastric ethanol infusion (iG) models now reproducing the clinically relevant pathologic spectra of ALD, such as mild or severe alcoholic steatohepatitis (ASH), alcoholic liver fibrosis, and alcoholic neutrophilic hepatitis (ANH).


Continued on page 7
The mission of the USC Proteomics Core is to make the cutting edge mass spectrometry technology available to the entire USC research community. While the core is a fee-for-service facility, it is also a research environment for multi-disciplinary research and education that utilizes mass spectrometry and other proteomics technologies to tackle complex biological and medical problems. It educates and provides support for users to design and tailor proteomics experiments to obtain high quality data for publications (see recent list of recent publications below) and grant proposals. The core also continually innovates on existing technologies.

The Core provides high-sensitivity and high-resolution mass spectrometry for protein and peptide analysis as its primary technology. The Core is a university-wide resource and is supported by funds from the Office of Provost, Keck School of Medicine and Center for Liver and Digestive Diseases. This state of the art facility was established and is headed by Dr. Ebrahim Zandi, associate professor of molecular microbiology and immunology and the faculty director of the Proteomics Core. The core is managed by senior technical expert, Dr. Yu Zhou. Services include protein identification and protein quantitation from a wide variety of sample types from simple mixtures (gel spots and bands) to complex mixtures (protein complexes, cell lysates, and plasma). The Proteomics Core is located in Hoffman Medical building (HMR 511/513) at the Keck School. Recently, a Q Exactive™ Hybrid Quadrupole-Orbitrap Mass Spectrometer and an EASY-nLC 1000 Liquid Chromatograph were added to the core equipment. The core also operates a LTQ Orbitrap XL™ ETD Hybrid Ion Trap-Orbitrap Mass Spectrometer and an Eksigent nanoLC 2D.

Examples of services provided by the core are sample preparation, including digestion of proteins in gel or solution, depletion of the most abundant serum proteins to study the protein differences in patients’ samples, identification of unknown proteins from gel pieces or solutions, characterization of protein post-translational modifications and identification of the modification sites. Commonly identified protein modifications include phosphorylation, deamidation, acetylation, methylation and ubiquitination. The core also provides quantitative protein and peptide analysis using TMT, iTRAQ, SILAC and/or label-free methods and bioinformatic analysis, including protein annotation and protein-protein interaction network analysis. A detail of services provided can be found on the core website: http://keck.usc.edu/Research/Centers_and_Programs/Proteomics_Core_Facility.aspx.

Selected Recent Publications with contribution from the core:


THE SOUTHERN CALIFORNIA RESEARCH CENTER FOR ALCOHOLIC LIVER AND PANCREATIC DISEASES

Continued from page 5


Metabolomics Core - This core provides routine and specialized services for metabolomic analyses in animal models and isolated cells. This core networks with the Animal Core to provide stable isotope-based metabolic profiling and flux analysis in animal models. This allows for the assessing of whole body- and tissue specific-metabolism, as well as metabolic cross-talk among tissues. Cell-type specific metabolomic analysis can be achieved in vitro, and ex vivo through interactions between Metabolomics Core and Non-Parenchymal Cell Core of the center. The core has successfully carried out metabolomic studies in hepatic macrophages, stellate cells, and tumor initiating cells. The Metabolomics Core is co-directed by Dr. Jun Xu (USC) and Dr. Paul Lee (UCLA), who combined, have 40 years of experience in metabolomic analysis. For more information about the Core’s services, please send an email to Dr. Jun Xu at junx@usc.edu.

For additional information on each of the ALPD & Cirrhosis research cores, please visit www.usc.edu/alpd.

RESEARCH DEAN’S CORNER

The research enterprise of the Keck School of Medicine is growing in size and complexity. To help lead our continued growth going forward, Dean Carmen A. Puliafito, MD, MBA, approved the creation of two new associate dean positions, one focused on clinical research and the other focused on basic and translational research. I am pleased to introduce to you the two individuals who have been recruited to the Keck School to assume these new leadership positions. Both individuals are accomplished researchers and research leaders. I look forward to working with them to continue the upward trajectory of research in the Keck School.

April Armstrong, MD, MPH
Associate Dean for Clinical Research

Dr. Armstrong came to the Keck School in June as associate professor in the Department of Dermatology, where she is vice chair for clinical research, director of the psoriasis program, and director of clinical trials and outcomes research. She brings a wealth of experience in clinical trials and outcomes research. She will apply that experience to two closely related leadership roles in clinical research — associate dean for clinical research in the Keck School and director of clinical research in the Southern California Clinical and Translational Science Institute.

As associate dean for clinical research, Dr. Armstrong will work to define the vision, goals and measures of success for clinical research within the Keck School. She will help to guide the development of an efficient and effective infrastructure that supports and promotes clinical research and integrates research with clinical care. She will play an important role in expanding the Keck School’s clinical research collaborations with other schools at USC and other academic and clinical institutions in Los Angeles and, where relevant, more broadly. She will also participate in the development and implementation of activities to enhance training and career development in clinical research within the Keck School and with other schools at USC. These activities will dovetail closely with her role as director of clinical research for the SC CTSI, where she will lead the development and operations of a new Clinical Research Support Office that will promote and support for investigator-initiated clinical trials.

Sarah Hamm-Alvarez, PhD
Associate Dean for Basic and Translational Research

Dr. Hamm-Alvarez joined the Keck School in July as professor in the Department of Ophthalmology, where serves as vice chair for basic research. In September, she will assume a new role for the Keck School as associate dean for basic and translational research. Her primary responsibility in this position will be to expand the scope and impact of basic and translational research conducted by faculty members and trainees within the Keck School. She will work with other research leaders in the Keck School and with basic, translational and clinical scientists to forge a highly effective, efficient operational framework that will foster fundamental discovery science and its translation to applications that improve human health. She will also work externally to establish academic, foundation and private-sector partnerships that will enhance the Keck School’s basic and translational research programs.
FACULTY AFFAIRS UPDATE

We are pleased to announce the following Keck faculty promotions:

Genevieve F. Dunton, PhD, MPH Associate Professor of Preventive Medicine and Psychology

Dr. Dunton joined the Department of Preventive Medicine in 2009. She received her PhD in psychology and social behavior from UC Irvine, her MPH from USC, and completed a cancer prevention fellowship at the National Cancer Institute. Dr. Dunton’s research focuses on health promotion, specifically the links between diet, physical activity and cancer risk. Her key innovation is the use of ecological momentary assessment (EMA), which enables study participants to self-report their activity and food intake in real time and relate this to precise locations by GPS. Dr. Dunton is applying EMA to examine activity in children, teens and adults. Her findings take into account not only total exercise, but also how the built environment and social environment influence physical activity in different populations. Dr. Dunton’s application of new technology puts her at the forefront of a rapidly-moving field. Her work is funded by grants from the NIH and the American Cancer Society, and she publishes frequently in the top journals in her field.

Amir Goldkorn, MD Associate Professor of Medicine

Dr. Goldkorn is a member of the section of genitourinary oncology in the division of oncology. After medical training and residency in medicine at UCLA, he moved to UCSF, where he completed a fellowship in hematology-oncology, and did additional post-doctoral work in the laboratory of Elizabeth Blackburn, the 2009 Nobel laureate. He joined the faculty of the Department of Medicine as an assistant professor in 2007. Dr. Goldkorn’s research and clinical focus is on biomarkers for cancer. Cancer is marked by formidable heterogeneity at every level, from patients, to tumor cells, to signaling pathways. To address this challenge, his research program focuses on three areas that offer unique opportunities to better understand and surmount cancer heterogeneity: circulating tumor cells (CTC), cancer stem cells (CSC), and telomerase activity. CTC and CSC are “hot” topics in current cancer research because they hold considerable promise for clinical use. To pursue this work, Dr. Goldkorn has been successful in securing major grant support from NIH and competitive private foundations. In particular, he is serving as PI on a multi-center prostate cancer clinical trial that was funded as an R01 last year. In 2011, Dr. Goldkorn founded the USC Norris Comprehensive Cancer Center Circulating Tumor Cell Research Core, where he serves as director. This core is an important resource for other clinical services to use CTC technologies in clinical trials.

Tracy C. Grikscheit, MD Associate Professor of Surgery

Dr. Grikscheit graduated from Harvard University, and pursued medical training at Columbia College of Physicians and Surgeons. She completed residency in general surgery and a research fellowship at Massachusetts General Hospital, followed by additional fellowship training in pediatric surgery at Seattle Children’s Hospital. In 2006, she joined the faculty of the Department of Surgery as an assistant professor. Dr. Grikscheit offers the rare combination of surgeon, teacher and scientist: her research on tissue engineering complements her clinical practice in pediatric surgery, and she trains pediatric surgeons & surgeons at CHLA. Early in Dr. Grikscheit’s career, she recognized the critical need for better therapies for children with intestinal failure, a not uncommon developmental deficit in neonates. She has since focused her research towards growing segments of intestine in vitro from stem cells harvested from patients. Dr. Grikscheit has successfully pioneered her approach in rodents and pigs, and is now on the verge of proposing human clinical trials. As evidence of the excitement and broad interest of her work, Dr. Grikscheit was featured on the front page of the New York Times in 2012. She has received two major grants from the California Institute for Regenerative Medicine (CIRM), as well as support from USC’s Coulter Translational Research Partnership and the Saban Research Institute.

Eugene S. Kim, MD Associate Professor of Surgery (Clinical Scholar)

Dr. Kim joined the faculty of the Department of Surgery in May of 2014 as an associate professor of clinical surgery. He is based at CHLA. Before coming to USC, Dr. Kim was associate professor of surgery at Baylor College of Medicine, where he had been a member of the faculty since 2007. Dr. Kim received his medical degree from Columbia University College of Physicians & Surgeons and completed a residency in general surgery at New York-Presbyterian Hospital, Columbia Campus. Dr. Kim spent two years as a fellow in pediatric surgery at Cincinnati Children’s Hospital Medical Center. Dr. Kim’s research and clinical emphasis is on pediatric surgical oncology, with a particular interest in care and treatment for children with complex solid tumors. His laboratory research addresses angiogenesis and cancer stem cells in pediatric neuroblastoma, the most common extracranial solid cancer in childhood. His work has been funded by the Children’s Neuroblastoma Cancer Foundation, St. Baldrick’s Foundation and by the NIH. Dr. Kim is editor-in-chief for the Journal of Case Reports and Clinical Research Studies and Recent Advancements in Pediatrics, and is a member of the editorial boards for eight additional journals. In addition to his work in pediatric oncology, Dr. Kim also specializes in surgical correction of chest wall deformities and anorectal malformations.
Chengyu Liang, PhD  Associate Professor of Molecular Microbiology and Immunology with tenure

Dr. Chengyu Liang was recruited to USC in 2009 as an assistant professor of molecular microbiology and immunology. Her research interests have focused on elucidating the roles of the UV-irradiation-resistance associated gene (UVRAG) in the regulation of autophagy and in viral entry, processes that may pave the way for novel anti-tumor agents as well as anti-viral agents for pathogens such as influenza, measles and the Ebola virus. She has been able to demonstrate that suppression of autophagy by the Bcl-2 oncogene product promotes the growth of breast tumor cells and that a viral version of the Bcl-2 oncogene (vBcl-2) is an important factor in the persistence and oncogenic properties of the human cancer-causing herpesvirus. These discoveries have the potential to add an entirely new approach to the treatment of cancer and viral infections. She has received several awards, including, the Leukemia & Lymphoma Society Fellowship Award, from 2007-2010, and her receipt of a Research Scholar award from the American Cancer Society, 2011-2015.

Keigo Machida, PhD  Associate Professor of Molecular Microbiology and Immunology with tenure

Dr. Keigo Machida was originally recruited to USC in 2006 as an assistant professor of research molecular microbiology and immunology. In 2008 he applied for and was selected by the Department to fill a tenure track assistant professor position. Dr. Machida has focused his research on the study of the hepatitis C virus (HCV) and its role in the etiology of hepatocellular carcinoma (HCC), one of the most deadly of all cancers. He has made critically important observations in the molecular study of the HCV envelope protein and the association of environmental factors such as alcohol and obesity in the development of HCV initiated HCC. His demonstration that toll-like receptor 4 induction by the non-structural 5A protein of HCV mediates alcohol-induced synergistic liver damage and the subsequent development of HCC, is of particular clinical impact. His further work has provided important molecular mechanisms for the roles played independently by alcohol and obesity in the development of HCC. Given the high world-wide prevalence of chronic HCV infection, and the major role of HCV in the development of HCC with its high rate of lethality, this work has substantial clinical significance. Dr. Machida's published work has appeared in the top specialty journals in the field including Hepatology, Gastroenterology, as well as more broadly based, higher impact journals such as Journal of Clinical Investigation and PNAS.

Nerses Sanossian, MD  Associate Professor of Neurology (Clinical Scholar)

Dr. Sanossian was recruited to the faculty of the Department of Neurology as a clinical instructor in 2004, after completing his medical training and residency in neurology at Albert Einstein College of Medicine, followed by a fellowship in vascular neurology at UCLA. Dr. Sanossian's research and clinical focus is on stroke, with a particular emphasis on pre-hospital therapy (by EMTs and paramedics) for patients who present with symptoms of stroke. Dr. Sanossian was instrumental in USC’s receipt of a $50 million gift from the Roxanna Todd Hughes Foundation to found the Roxanna Todd Hodges Transient Ischemic Attack clinic. He carries significant clinical responsibilities as medical director of the LAC+USC Stroke Clinic and the newly established stroke clinic at USC Verdugo Hills Hospital. Dr. Sanossian teaches medical students, residents and fellows. He has served as director of research in the neurology residency program, and is the founding director of the USC Stroke Fellowship program, accredited by the ACGME. Dr. Sanossian has been celebrated as Teacher of the Year for the Department of Neurology in 2007, 2009, 2012, and 2013. In 2010, he was also recognized with a Year IV Student Teaching Award.

Fredrick Schumacher, PhD  Associate Professor of Preventive Medicine with tenure

Dr. Fredrick Schumacher joined the faculty of the Keck School of Medicine in the Department of Preventive Medicine as an assistant professor on the tenure track in 2008. His research has centered around how environmental factors and genetics contribute to cancer risk, with emphasis on cancers of the colon, breast, and prostate. He has used GWAS (genome-wide association studies) to focus on both the initiation event in the development of cancer, as well as the effect of environmental factors, distinct metabolic traits and biomarkers on risk assessment and disease progression. He has developed resources to evaluate the clinical impact of genetic risk modeling, particularly in the approaches to clinical trials. Of particular importance, he has been successful in identifying multiple novel susceptibility loci associated with breast, prostate, colorectal, and germ cell tumors using the GWAS approach, and he has extended this work to include SNP analysis to more finely map the loci.

Continued on page 10
Amytis Towfighi, MD Associate Professor of Neurology (Clinical Scholar)

Dr. Towfighi was recruited to the faculty of the Department of Neurology in 2007 as an assistant professor of clinical neurology, based at Rancho Los Amigos National Rehabilitation Center. Dr. Towfighi earned an MD from Johns Hopkins School of Medicine, and then completed neurology residency at Harvard/Massachusetts General Hospital and Brigham and Women’s Hospital. After residency, she spent an additional year in a vascular neurology fellowship at UCLA before joining the faculty at USC. She established and directs a new acute neurology unit at Rancho, where she also serves as chair of the Department of Neurology and associate chief medical officer. In 2014, Dr. Towfighi was appointed as director of neurological services and innovation for the Los Angeles County Department of Health Services. In addition to her administrative roles, Dr. Towfighi maintains an active research program in stroke intervention and health disparities research. In one arm of her research program, she studies the epidemiology of stroke, with an emphasis on gender disparities. Dr. Towfighi’s more recent research emphasizes community-based interventions to reduce the incidence of stroke. The focus is on lifestyle practices (healthy eating, regular exercise) with outpatient clinical mentoring in stroke patients. She has been recognized with a number of awards, including the Michael S. Pessin Stroke Leadership Prize from the American Academy of Neurology in 2013, and the Robert G. Siekert New Investigator Award in Stroke from the American Heart Association in 2012.

Guy Young, MD Professor of Pediatrics (Clinical Scholar)

Dr. Young joined the faculty of the Department of Pediatrics as associate professor in 2002. He was appointed as a clinical scholar in 2011, and currently serves as director of the Hemostasis and Thrombosis Center at CHLA. Before coming to USC, Dr. Young was assistant professor of pediatrics at the University of Maryland, Loma Linda University, and at UCLA. Dr. Young received his MD from SUNY Stony Brook, and completed a residency in pediatrics at the Long Island Jewish Medical Center. He then trained as a fellow in pediatric hematology/oncology at the Children’s National Medical Center of the George Washington University School of Medicine. Dr. Young’s research focuses on clotting disorders, both those where clotting is insufficient (hemophilia) and those where it is excessive (venous thrombosis). His clinical research emphasis is on the use of thromboelastography to monitor clot formation. As a relatively new clinical modality, there has been a need to develop standards for thromboelastography, and Dr. Young has led a working group to develop such standards. He has also participated in efforts to introduce a novel clotting agent (bivalirudin) for clinical use in children. Dr. Young’s research on thromboelastography received support from Novo Nordisk and GlaxoSmithKline. Dr. Young gives frequent presentations for patients and their families. In 2013, he was selected as Physician of the Year by the National Hemophilia Foundation.

Jeffrey C. Wang, MD Professor of Orthopaedic Surgery and Neurological Surgery (Clinical Scholar)

Dr. Wang joined the faculty in 2013 as professor of clinical orthopaedic surgery and neurological surgery. Previously, he had served as professor of orthopaedic surgery and neurosurgery at UCLA, where he was chief of spine service and executive director of the Comprehensive Spine Center. Dr. Wang received his MD from the University of Pittsburgh School of Medicine. He was a resident in orthopaedic surgery at UCLA, and spent a fellowship year at Case Western Reserve University. In 1997, Dr. Wang returned to UCLA as an assistant professor. Dr. Wang’s research complements his clinical focus on surgical treatment of spine disorders. He is active in studies to improve bone regeneration and spinal fusion surgery as a treatment for intervertebral disc degeneration. His laboratory is also pursuing work on growth factors and stem cells as possible therapeutic targets for regeneration of the intervertebral discs. This is an important clinical problem, since disc degeneration is common with aging, and a major source of pain and disability in older adults. Since his arrival at USC, Dr. Wang has established a combined orthopaedic surgery/neurosurgery spine surgery fellowship.

FUNDING OPPORTUNITIES?

Are you currently looking for funding opportunities? For a listing of current extramural and intramural funding opportunities, please visit: http://www.usc.edu/schools/medicine/school/offices/resadv/newsletter/funding.html.

USC Office of Research has implemented a new simpler portal for submission of internal research proposals (http://uscapplicationportal.weebly.com/), including both external proposals that are institutionally limited and internal funding programs, such as Zumberge and the Collaboration Fund. As in the past, these competitions will all be listed at http://research.usc.edu/for-investigators/funding/.

E-TOOLS FOR CLINICAL RESEARCH

USC Health Sciences Profiles is an expertise discovery and research collaboration tool. http://profiles.sc-ctsi.org/search/

The Clinical Studies Directory features more than 300 active clinical studies at USC. The current site is in English; the front pages are also available in Spanish and Mandarin Chinese. http://clinicaltrials.keckmedicine.org/

The Research Training Finder is designed to help researchers, staff members and trainees access the large body of courses available to help them do their jobs better and meet the increasingly complex requirements for research compliance at USC. http://researchtrainingfinder.usc.edu/
As you are probably aware, the Uniform Guidance (also referred to as A-81) went into effect on December 26, 2014. The Uniform Guidance was issued by the Office of Management and Budget (OMB) and was intended to streamline the administration and operation of federal awards while increasing the government’s oversight. The Uniform Guidance replaced eight different circulars, including A-21 - Cost Principles for Educational Institutions. The Uniform Guidance does not change the core principles of what costs can be charged to a federal award. Costs still must be necessary, reasonable, allocable, allowable and consistently treated. However, certain changes have been made in specific areas, including:

- Charging of administrative/clerical salary costs;
- Charging of computing devices under $5,000;
- Treatment of participant support costs;
- Treatment of visa costs; and
- Subawards, including a de minimum of 10 percent F&A.

For more information on these changes, please review the A-81 (Uniform Guidance) Quick Guide posted on the Office of Research website: https://research.usc.edu/files/2011/07/A-81-Quick-Guide-2.20.15.doc.

You may also review presentations from recent Research Administrators Forums on this topic. An overview on implementation was presented at the November 4, 2014 meeting and changes to the treatment of subawards was covered in the March 31, 2015 Forum: http://ooc.usc.edu/research-administrators-forum.
KECK RESEARCH ACCOMPLISHMENTS:
APRIL - JULY 2015

ACADEMY & SOCIETY FELLOWS

DAVID BARON
Professor of Psychiatry
Distinguished Life Fellow – American Psychiatric Association

Laurie DeLeve
Professor of Medicine
Fellow – American Association for the Study of Liver Diseases

John Louie Go
Assistant Professor of Radiology and Otolaryngology
Fellow – American College of Radiology

Neil Kaplowitz
Professor of Medicine
Fellow – American Association for the Study of Liver Diseases

INTERNATIONAL AWARDS AND DISTINCTIONS

Sabb Quidway
Distance Education Operations Specialist, Department of Family Medicine
2015 Distinguished Educator – Apple

Paul Thompson
Professor of Neurology, Psychiatry, Radiology, Ophthalmology
Innovations in Academia – University of Kent

NATIONAL AWARDS AND DISTINCTIONS

David Baron
Professor of Psychiatry
2015 Harry Stack Sullivan Award – Johns Hopkins School of Medicine and Sheppard-Pratt Health System

Kathryn Challoner
Voluntary Faculty in Emergency Medicine
2015 Humanitarian Award – California Chapter of the American College of Emergency Physicians

Erick Etting
Assistant Professor of Clinical Emergency Medicine
2015 Leadership Award – AMA Foundation

David Hinton
Professor of Pathology
George K. Smelser Endowed Lectureship – Columbia University

Josseh Javad
Associate Professor of Radiology and Biomedical Engineering
Appointed President – Society of Nuclear Medicine and Molecular Imaging

Jay R. Lieberman
Professor of Orthopaedic Surgery
Appointed President – American Association of Hip and Knee Surgeons

Janos Peti-Peterdi
Professor of Physiology and Biophysics
2015 Young Investigator Award – American Association for the Advancement of Science

Brent Polk
Professor of Pediatrics
2015 Shwachman Award – North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition

UttaM Sinha
Associate Professor of Otolaryngology
Joseph H. Ogura Memorial Lecture – American Society of Otolaryngology and the American Heart Association

INTERNAL AWARDS

Paula Cannon
Associate Professor of Molecular Microbiology and Immunology
2015 Pew-Stewart Scholar for Cancer Research

Jo Marie Reilly
Associate Professor of Clinical Family Medicine
2015 Pew-Stewart Scholar for Cancer Research

Peter Crocke
Professor of Surgery
Arnold P. Gold Foundation Leonard Tow Humanism Award

AL AWARDS AND DISTINCTIONS

Paula Cannon
Associate Professor of Molecular Microbiology and Immunology
2015 Pew-Stewart Scholar for Cancer Research

Jo Marie Reilly
Associate Professor of Clinical Family Medicine
2015 Pew-Stewart Scholar for Cancer Research

Peter Crocke
Professor of Surgery
Arnold P. Gold Foundation Leonard Tow Humanism Award

INTERNAL AWARDS

Jeffrey Cancenko
Assistant Professor of Clinical Medicine
Kaiser Excellence in Teaching Award – Clinical Science

Peter Crocke
Professor of Surgery
Arnold P. Gold Foundation Leonard Tow Humanism Award

INTERNAL KECK GRANT COMPETITIONS

KSOM faculty members competed for special Keck grant competitions. Recent awards went to:

Wright Foundation

Pinghui Feng (USC Norris)
Targeting IKKepsilon to Boost T Cell Antitumor Immunity Against Melanoma

Parveen Garg (Medicine)
Noninvasive Coronary Endothelial Function Assessment using Arterial Spin Labeling

Kevin King (Radiology)
Pilot Translational Study of Sonazoid-Enhanced Ultrasonography for Sentinel Lymph Node Mapping in Cutaneous Melanoma

Núria Pastor-Soler (Medicine)
Novel Pathways for Detection and Inhibition of Kidney Cancer Metastasis

Mary Yamashita (Radiology)
Emerging Tools in the Detection of Breast Cancer: Comparison of Contrast Enhanced Spectral Mammography with Digital Breast Tomosynthesis to Conventional Imaging Techniques including Contrast Enhanced Magnetic Resonance Imaging and 2D Mammography with or without Targeted Ultrasound

Donald E. and Delia B. Baxter Foundation

Jon-Paul Pepper (Stem Cell Biology and Regenerative Medicine)
Treatment of neuromuscular atrophy via transplantation of human stem cell-derived motor neurons

Min Yu (Stem Cell Biology and Regenerative Medicine)
Molecular characterization of metastatic breast cancer stem cells with tissue tropism

Kevin S. King (Radiology)
Cerebrovascular reactivity as an early predictor of brain hypoperfusion, microvascular injury, and cognitive decline

Keck School of Medicine Contributors

Tom Buchanan, M.D.
Vice Dean for Research

Judy Garner, Ph.D.
Vice Dean for Faculty Affairs

Janet Stoeckert
Manager, Special Projects

Rene Pak
Associate Director, Operations

Donald E. and Delia B. Baxter Foundation

Jon-Paul Pepper (Stem Cell Biology and Regenerative Medicine)
Treatment of neuromuscular atrophy via transplantation of human stem cell-derived motor neurons

Min Yu (Stem Cell Biology and Regenerative Medicine)
Molecular characterization of metastatic breast cancer stem cells with tissue tropism

Kevin S. King (Radiology)
Cerebrovascular reactivity as an early predictor of brain hypoperfusion, microvascular injury, and cognitive decline

Keck School of Medicine Contributors

Tom Buchanan, M.D.
Vice Dean for Research

Judy Garner, Ph.D.
Vice Dean for Faculty Affairs

Janet Stoeckert
Manager, Special Projects

Rene Pak
Associate Director, Operations

Design

Health Sciences Public Relations & Marketing