Dear Keck Colleagues,

Welcome to the Keck Research Quarterly, a new publication from the Office of Research in the Keck School of Medicine. The Quarterly is designed to give you an in-depth look at research in the Keck School to complement our weekly notices about funding opportunities in the Keck Research Funding Update, and seminars and lectures in the Keck Research Events Update.

In this inaugural issue we are proud to feature Faculty Spotlight, the first in a series of profiles on our leading researchers, this one highlighting the research and accomplishments of David Hinton, M.D. and his study of age-related macular degeneration. We are also pleased to introduce you to our first installment of Managing your Research that provides readers with practical information on preparing, submitting and managing research grants, and running a research operation in the Keck and USC environments. A section on What Faculty Need to Know provides information and advice that will help with professional development in the Keck culture and should be of particular value to new faculty members. Finally, the Keck Research Accomplishments section will highlight the many outstanding things Keck faculty members do. This quarter’s Accomplishments highlights significant awards received by faculty since 2013 and summarizes our success in garnering extramural grants in FY14.

My team and I hope you enjoy this and subsequent issues of the Keck Research Quarterly. If you have suggestions for making this publication more useful to you and your fellow faculty members, please let me know.

Tom Buchanan, M.D.
Vice Dean for Research

Dr. David Hinton’s research is focused on developing novel therapies for age-related macular degeneration (AMD) – the leading cause of irreversible blindness in the elderly. He is approaching this goal in two main ways: (1) restorative cell therapy to replace cells already damaged, and (2) neuroprotection to prevent the retinal degeneration. A primary site of pathology in AMD is the retinal pigmented epithelial cell (RPE). Dr. Hinton has been studying the basic biology of the RPE and its response to injury for over 20 years. He established the importance of RPE-derived growth factors in AMD and other retinal disorders including vascular endothelial growth factor (VEGF), connective tissue growth factor (CTGF) and hepatocyte growth factor (HGF). He has developed a well-known in vitro model of polarized RPE cell monolayer culture and has established several in vivo models that recapitulate several features of the pathophysiology of AMD. He has developed (in collaboration with Dr. Mark Humayun at USC and Dr. Dennis Clegg at UC Santa Barbara) a novel cell therapy approach to the late, dry form of AMD. Embryonic stem cells are differentiated into RPE and then grown as a polarized monolayer for subretinal implantation in patients. With extensive funding from the California Institute for Regenerative Medicine (CIRM), this team is completing preclinical studies demonstrating safety and efficacy of the approach. They are planning to submit an investigational new drug (IND) application to the FDA this fall and have already obtained funding to begin a Phase 1 safety trial in AMD patients in 2015.

Dr. Hinton has also established a program to develop drugs that would protect RPE cells and light sensitive photoreceptors from damage. Such drugs could be used as a preventative measure or in conjunction with cellular therapy. Hinton is particularly interested in the small heat shock protein alphaB-crystallin. He has shown that it strongly protects RPE from oxidative

Continued on page 2
I initially studied tumors of the nervous system in which mechanisms of represented an approachable part of the research program for Neurosurgeons at the time of brain surgery. I was trained as a board-certified Neuropathologist whose main role was to evaluate tissue samples obtained by biopsy from patients with various neurological diseases. I was interested in establishing a research program to study the biology of the RPE and the potential for molecular therapies to treat retinal diseases.

I was very fortunate to work with Dr. Florence Hoff in the Department of Pathology. Dr. Hoff introduced me to the field of neuroimmunology and among our studies was a paper in Journal of Experimental Medicine that demonstrated the expression of tumor necrosis factor in the brains of patients with multiple sclerosis. I went on to develop collaborations with Drs. Steve Stohlman and Corvi Bergmann at Cleveland Clinic where we were funded by NIH to study the role of immunoregulatory molecules in animal models of demyelination for over 20 years. The expertise I developed in these projects has been very influential in developing concepts about the role of inflammation in AMD.

A third major area of collaboration has been with Dr. J. Ambati at the University of Kentucky. This collaboration developed as a result of my expertise in the culture and evaluation of human RPE. Over the past five years I have co-authored seminal papers with him on the basic pathogenesis of AMD in PNAS, Cell, Nature Medicine, and the New England Journal of Medicine. You also oversee the Cell and Tissue Imaging Core. Could you describe some of the resources of this core and how others USC investigators can benefit from its use?

The Cell and Tissue Imaging Core Facility is available for research projects requiring specialized microscopy. The cell and tissue imaging core is currently supported by a National Cancer Institute (NCI) Core grant to the Norris Cancer Center. The Cell and Tissue Imaging Core is available upon appointment, 24 hours/day, seven days per week. The primary function of the Core is to provide assistance and training in the operation of equipment for laser scanning confocal microscopy, multiphoton laser scanning confocal microscopy, and light microscopy.

What would you say is the most significant advance in this field as contributed by your own research?

I have been a leader in establishing the critical role of the RPE in the pathogenesis of AMD. I was the first to show expression of Vascular Endothelial Growth Factor (VEGF) in RPE from AMD patients with the wet form of the disease in 1996. Since that time, anti-VEGF therapies have revolutionized the treatment of these patients. I have promoted the concept of RPE function as a polarized monolayer, and have established in vitro models of RPE monolayer formation. I initiated the original studies at USC to differentiate embryonic stem cells into RPE and established a collaboration with Dr. Mark Humayun to form a team of investigators that have gone on to develop a cellular therapy for AMD that may soon be in clinical trials. I am developing novel neuroprotective therapies that could help to prevent the progression of retinal degeneration in patients with AMD.

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

When I was recruited to USC, I was very fortunate to continue collaboration with my postdoc mentor, Dr. Carol Miller. My first paper at USC was a first author publication in the New England Journal of Medicine (coauthored by Dr. Carol Miller and Dr. Alfreds Sadora). In this paper we described for the first time a retinal degeneration in patients with Alzheimer’s disease. Since that time, over 300 publications have been written that further evaluate this change and its potential in using the eye as a “window to the brain.” In exciting recent studies, we are continuing this work using novel technologies with collaborators at Cedars Sinai.

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What do you think will be the next big advances in your field and what do you think USC can do to position itself to be a leader in this field?

There are going to be rapid advances in the prevention and treatment of blindness, including regenerative cellular therapy (not only of the RPE but also the photoreceptors and potentially the retinal pigment epithelium, and neuroprotective therapies (to prevent retinal degeneration). Dr. Mark Humayun is leading a NIH-funded effort with Dr. Stephen Ryan, who introduced me to the field of opHTalmology, to develop small peptides of alphaB-crystallin (one of my former graduate students Andrew MacKay from USC School of Pharmacy) to develop exosomes where it can protect adjacent cells. Dr. Hinton has gone on to develop a cellular therapy for patients with AMD or other retinal degenerations. Dr. Hinton has established a collaboration with Dr. Mark Humayun to form a team of investigators that have gone on to develop a cellular therapy for AMD that may soon be in clinical trials. I am developing novel neuroprotective therapies that could help to prevent the progression of retinal degeneration in patients with AMD.

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**MANAGING YOUR RESEARCH**

**Electronic Grant Submission**

Electronic Grant Submission Routing and Approvals has arrived at Keck Kuali Coeus or “KC” for short is the new USC grant and contract proposal submission and development module of Total Access Research Administration (aka TARA). KC is being rolled out to Keck School of Medicine in three phases: (1) routing and approval of grant applications, (2) budget development, and (3) system-to-system submission via grants.gov. A “soft launch” of phase 1 is currently underway in the Keck School, meaning that use of the system is optional for the time being. Starting November 1 however, all Keck proposals are required to be routed through the KC system. All department administrators and many faculty members have already completed training on KC for phase 1. Faculty can log in to TARA/KC, review and affirm the project details (including personnel effort), and let the system route the proposal through Keck and USC approvals before it is submitted to the sponsor. This electronic process in the KC system replaces the paper PAR form. Eventually, it will be the required method for routing and approval of grant applications throughout USC, so we recommend that you become familiar with it soon if you are a grant-submitting PI.

On-line training materials including a training video are available at [https://research.usc.edu/kuali-coeus-kc](https://research.usc.edu/kuali-coeus-kc). Assistance is also available through the Keck Office of Research Administration (Keck KC Help Desk at 442-5915) during regular business hours.

**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](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/](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/](http://research.usc.edu/for-investigators/funding/).

**Where Do I Go For Research Contacts?**

Go to The Guide to Research Services and Process at USC for a directory of frequently needed research contacts: [https://research.usc.edu/files/2011/07/Who-Do-I-Call-If-SC-Contact-list_REVISED-3-31-14.pdf](https://research.usc.edu/files/2011/07/Who-Do-I-Call-If-SC-Contact-list_REVISED-3-31-14.pdf)

**INTRODUCING “CLIN CARDS” FOR RESEARCH PARTICIPANTS**

ClinCards are reloadable debit cards for industry and non-industry clinical trials and research studies and is the preferred method of paying human subjects for recurring visits. The use of the ClinCards will eliminate the need for cash advances. These debit cards can be used for point of sale purchases with merchants that accept MasterCard, for bank teller withdrawals, and for ATM transactions. Normally, there is a fee for new ClinCards and a fee every time the card is loaded with a new amount. The Keck School of Medicine will absorb these costs to encourage the use of the cards.

The benefits of the card are:

- Payment to the subject is instant
- More secure than receiving cash
- No bank account is required
- Personal information is kept secure since no social security number is required
- No fee when using the card for purchase as a debit/credit or bank teller withdrawal

For more information on the ClinCard program, please contact Gabe Ariza, Program Coordinator for USC Corporate Card Services. ariza@usc.edu, (213) 740-6015.

**MORE RESEARCH TRAINING FOR MY STAFF AND ME**

In cooperation with the SC Clinical and Translational Science Institute, a new “Research Training Finder” has been created at [http://sc-ctsi.org/training-matrix/](http://sc-ctsi.org/training-matrix/). Use this website to quickly determine what training is required for you, your staff and your students, based on the type of research that you do.

The Center for Excellence in Research (CER) program has grown to 23 events this fall, coupled with a new grant mentoring/review program. Please go to: [http://research.usc.edu/for-investigators/training/](http://research.usc.edu/for-investigators/training/) for the current schedule of events. In addition, there are special training opportunities for clinical research coordinators in partnership with the SOCRA organization and on-line training in clinical research at USC.

**KECK GRANT AWARDS AND PROPOSALS: FISCAL YEAR 2014**

Total grant awards made to Keck School of Medicine reached $203M in FY14, a 6.7% increase over FY13. NIH grants totaled $135M, an increase of 12% over FY13. (See graph).

The dollar value of grant proposals submitted by Keck decreased by 5% from $367M in FY13 to $348.6M in FY14.
For more information about research at the Keck School of Medicine of USC, contact (323) 442-3568.

Keck School of Medicine
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