# USC Southern California Research Center for ALPD and Cirrhosis JOINT SYMPOSIUM with the UCSD/UCLA DERC

Keck School of Medicine of the University of Southern California  
McKibben Hall (MCH), Room 149, Health Sciences Campus  
1333 San Pablo Street, Los Angeles, CA 90033, Info: (323) 442-3121 or handan@usc.edu  
**DECEMBER 4, 2009 at USC in Los Angeles**

**8:30-9:00**  
Continental Breakfast

**9:00-9:10**  
Welcoming Remarks, Hide Tsukamoto, DVM, Ph.D.

### Mechanisms of Liver Metabolism and Fatty Liver

**9:10-9:35**  
Barry M. Forman, Ph.D., Professor and Director, Gene Regulation & Drug Discovery, The Beckman Research INST., City of Hope Med Center  
“FXR and Hepatic Metabolism: on the Fast Track”

**9:40-10:05**  
Marc Montminy, Ph.D., Professor, Clayton Foundation, The Salk Institute  
“Regulation of Hepatic Gluconeogenesis by the TORC/CRTC Family of CREB Coactivators”

**10:10-10:35**  
Mark Czaja, M.D., Professor of Medicine, Albert Einstein College of Medicine  
“Regulation of Cellular Lipid Accumulation by Macroautophagy”

**10:40-10:55**  
Break

**11:05-11:20**  
Kuk-Wha Lee, M.D., Ph.D., Assistant Professor of Pediatrics, UCLA  
“Contribution of the Growth Hormone/Insulin-Like Growth Factor Axis in the Pathophysiology of Hepatic Steatosis”

### Pilot Projects

**11:25-11:40**  
Ekihiro Seki, M.D., Ph.D., UCSD  
“TLR Signaling in ASH vs. Non-ASH”

**11:45-12:00**  
Kinji Asahina, Ph.D., USC  
“Hepatic Stellate Cell Precursors in Developing and Fibrotic Livers”

**12:05-12:20**  
Jenny Yuan, Ph.D., UCLA/West LA VA  
“The Role of Protein Kinase D in Alcoholic Pancreatitis”

**12:25-12:40**  
Bernd Schnabl, M.D., UCSD  
“Early Bacterial Translocation in Alcoholic Liver Injury”

**12:45-13:35**  
Lunch

**13:45-13:55**  
Special Remarks: Samir Zakhari, Ph.D., Director, Division of Metabolism and Health Effects, NIAAA/NIH

### Oxidant Stress, Inflammation, and Cancer

**14:30-14:55**  
David Brenner, M.D., Vice Chancellor for Health Sciences, Dean, UCSD School of Medicine  
“ROS, NADPH oxidase, and liver fibrosis”

**15:00-15:25**  
Neil Kaplowitz, M.D., Professor and Director, USC Research Center of Liver Disease  
“Mitochondrial and ER stress Coupling”

**15:30-15:55**  
Hide Tsukamoto, DVM, PhD, Professor and Director, ALPD and Cirrhosis Research Center  
“NASH Models”

**16:00-16:20**  
Keigo Machida, Ph.D., Assistant Professor, Dept of Mol. Microbiology and Immunology, USC  
“Liver Cancer Stem Cells Generated by HCV, Alcohol, and Obesity”

**16:25-16:40**  
Break

**16:40-17:05**  
Jerome Rotter, M.D., Professor, Pediatrics and Human Genetics, UCLA/Cedars Sinai  
“Genome-Wide Association of IBD -- From Susceptibility to Therapy”

**17:10-17:35**  
Anna Gukovskaya, Ph.D., Professor and Senior Career Scientist, UCLA, West LA VA  
“Autophagy in Pancreatitis”

**17:40-18:00**  
Simon Beaven, M.D., Instructor, Gastroenterology, UCLA  
“LXR Signaling in Hepatic Inflammation and Fibrosis”

**18:05-18:15**  
Closing Remarks, Jerry Olefsky, M.D.

**18:30-20:30**  
Reception and Dinner in the Seaver Residence Hall
DERC P&F Grant Announcement

2010 Pilot and Feasibility Projects in Endocrinology & Diabetes

Pilot & Feasibility Program, Director: Pinchas Cohen

As part of the ARRA Funds awarded to our UCSD/UCLA DERC grant, the Pilot and Feasibility grant program will support ~8 grantees at approximately $30,000-$40,000 per year for 2010, double the number normally available. Thus, the 2010 competition will award $300,000 in awards for P&F.

Applications DUE March 5th 2010
to Dr. Pinchas Cohen at: hassy@mednet.ucla.edu

As part of the UCSD/UCLA DERC grant, a mechanism to fund innovative new projects that will explore the feasibility of novel testable concepts and enhance the endocrine/diabetes research scope within the institutions is again available. A special emphasis on promoting promising junior faculty involved with diabetes research is key to the UCSD/UCLA P&F mission. It is expected that P&F studies will generate preliminary data that will be used by these investigators in diabetes/endocrinology-related RO1 applications in the years following their award.

P&F grant format

Failure to meet the requirements for grant format will lead to an administrative disqualification of the proposal. The P&F grant applications should include:

(a) Face page with the title of the grant, the name, email, academic title, department, and institution of the PI, the names of additional personnel and collaborators and a 200 word abstract.

(b) Biosketches for the PI and other key personnel.

(c) The scientific proposal (5-page limit).

(d) References.

The entire grant must be submitted as a single emailed pdf file less than 2 megabite in size. If the grant includes high-resolution images, these must be reduced to meet the size requirement. Failure to provide a single pdf file or a file that is too big will result in disqualification. No budget is required, but the scope of the work should be appropriate for 1-year project and the funds cannot be used for the PI salary.

Eligibility

All eligible investigators must have faculty appointments at UCLA, Salk, Cedars, or UCSD and be independent investigators. To be eligible for a P&F grant you need to be eligible to submit an RO1 as a PI at the end of the grant period. A joint appointment at an affiliated institution is allowed. Investigators eligible for pilot and feasibility funding generally will be expected to fall into three categories:

(Category 1) New investigators without current or past non-mentored NIH research support as a principal investigator (current or past support from other sources being modest).

(Category 2) Established investigators with no previous work in diabetes that wish to apply their expertise to a problem in this area.

(Category 3) Established investigators in diabetes/endocrinology research who propose testing innovative ideas that represent clear departure from ongoing research interests.

Interactions with other DERC components

It is expected that junior faculty will be able to rely on the advice and support of a senior DERC investigators and will have a priority access to DERC Cores, including an opportunity to discuss their projects in depth with the core directors in order to receive maximum benefits from their services. Similarly, investigators with no previous experience in diabetes/endocrinology research will be expected to have a DERC collaborator. P&F grantees will be encouraged and expected to utilize DERC core resources.

Final report and presentation at the annual retreat

A report on each pilot and feasibility study conducted will be due at the end of the study period and an update will be requested yearly for four years after the completion of the award. These brief reports will contain professional career status at the time of the award and at the time of the report; an overview of the project including its significance and salient results; a list of resulting publications; and peer-reviewed subsequent funding in the same or related areas. Funded P&F investigators will be expected to attend the annual DERC retreat as well as in a meeting of Regional P&F awardees, and present the results of their work in the year immediately following their award. Travel to these meetings will be charged to the individual P&F awards. ALL PAPERS MUST CITE P30 DK063491

Notification procedure:

After approval of the funding decisions by the DERC executive committee, funded and unfunded investigators will be notified and, when appropriate, a brief summary of the reviews will be sent to them by email (not a detailed critique). Expected activation date is 5/1/2010.
**REPORT: Clinical Investigation Institute/Nature Medicine Mtg**

**Bench to Bedside: Metabolism; October 8-10, 2009**

On October 8-10, 2009, an outstanding meeting was hosted by Nature Medicine and UCSD focused on Metabolic Diseases. The meeting was held at the Hilton Torrey Pines in La Jolla and featured a stellar group of speakers, including: Gokhan Hotamisligil, Peter Libby, Helen Hobbs, Michael Karin, Steve Shoelson, Paresh Dandona, Gerry Shulman, Ira Goldberg, Philipp Scherer, Barbara Kahn, Christopher Newgard, Tony Lam, Zofia Zukowska, Daniel Drucker, David Cummings, and Francesco Rubino. The meeting was divided into several interrelated sessions, including: (1) Lipids and Atherosclerosis, (2) Metabolic Disease and Inflammation, (3) Muscle Function and Metabolism, (4) Mechanisms of Obesity, (5) CNS Hormone Regulation, and (6) Diabetes/Metabolic Surgery. In addition to the invited speakers, over 100 abstracts were submitted to the meeting. Several were selected for short talks given during the program and the others were exhibited as poster presentations. The meeting spanned a wide range of research in metabolic diseases, ranging from very basic investigation all the way up to clinical research, including the use of bariatric surgery to treat diabetes. This range of talks revolved around the theme of the overall program, which was Bench to Bedside Research in Metabolism. Wolfgang Dillmann and Jerrold Olefsky from our UCSD/UCLA DERC, as well as Gary Firestein, were the organizing Committee from UCSD, partnering with Juan Carlos Lopez and Randy Levinson from Nature Medicine.

**Keynote Speaker:**

**Michael Brown**

(U Texas)

The highlight of the meeting was the opening Keynote Presentation by Dr. Michael Brown. His talk covered 30 years of research from the Brown and Goldstein lab, and was a true tour de force. The science underlying his talk was at the absolutely highest level and the presentation itself was magnificent. He discussed their Nobel prize-winning work on the discovery of the LDL receptor, its regulation by intracellular cholesterol levels and how this led to the recognition of Familial Hypercholesterolemia. Their findings were instrumental in the discovery and development of HMG-Co-A reductase inhibitors ("statins"), which are the most widely prescribed pharmaceuticals in the world. Dr. Brown then went on to describe their work on the detailed mechanisms of intracellular cholesterol regulation through the coordinated interactions between SREBP, SCAP, and INSIG1. Junior faculty and fellows attending were inspired, and many commented that this talk motivated them to fully pursue careers in biomedical science. Based on the success of this symposium, it is likely that Nature Medicine will go on to sponsor another meeting on this topic within the next two years. This meeting was immediately followed by the Western Section DERC symposium in the same hotel, which contributed to the success of our DERC meeting.

**Meeting REPORT: The First Western DERC Meeting**

Oct. 10, 2009; Keynote Speaker: Professor Ron Evans, Salk Institute

In an effort to advance the scientific and mentoring collaborations among the four Western DERCs, initiated a new venue for early career investigators who received a P&F grant from their DERC in which members of the four Western DERCs (UCSD/UCLA, University of Washington, Baylor College of Medicine, and University of Colorado at Denver) interacted and presented data. Over seventy DERC members attended the meeting, which began with a superb presentation by Dr. Ron Evans and included 10 outstanding oral presentations (two each from the five Universities), followed by a Wine & Cheese Poster session. The general feedback from the attendees suggests that the forum was a great success and allowed enriching interactions and discussions. We expect to hold similar meetings in collaboration with these institutions in the future. **Organizer: Dr. Pinchas Cohen.**
The DERC Transcriptional Genomics Core is a state-of-the-art facility that facilitates high throughput genomic experimentation. Data acquisition and analysis require expensive instrumentation and reagents and a highly skilled team of individuals who are experts in specific components of the overall procedure. These technologies therefore lie beyond the scope of most individual laboratories. The DERC Transcriptional Genomics Core (comprised of the Biomedical Genomics Microarray (BIOGEM) and VA Gene Chip Facilities at UCSD) has been instrumental in providing DERC investigators access to genomics technologies for over 10 years. This includes Microarray studies using Illumina, Agilent, Nimblegen and Affymetrix platforms and next-gen sequencing using Illumina (Solexa) and Roche (454) technologies. The Core contains three ‘Illumina 1G Analyzer instruments’ in addition to a ‘Roche 454 Genome Sequencer FLX Instrument’.

The Illumina 1G Analyzer (Solexa) is based on the massively parallel sequencing of millions of fragments using a proprietary clonal single molecule array technology coupled to a novel reversible terminator-based sequencing chemistry. For short sequence reads, the approach has been determined to be highly robust and accurate. Applications in whole-genome association studies, expression analysis, and sequencing in addition to genome wide location studies have been reported. Read lengths, are currently up to 150 bp in length. The Roche (454 Life Sciences) sequencing technology is capable of sequencing 500 million bases in a ten-hour period. In this method DNA is amplified using a ‘clonal’ emulsion bead PCR approach and DNA is pyrosequenced using a micro-fabricated, massively parallel platform. This generates sequencing reads 500 bp in length. Amongst others, applications in genome and transcriptome sequencing, sequence capture targeted region analysis, and small RNA, have been reported.

**SERVICES**

1. Expression microarray technology; Affymetrix, Agilent, NimbleGen, and Illumina microarray platforms for analysis of large scale gene expression.
2. MicroRNA analysis using Agilent, Invitrogen NCode and Exiqon microarray platforms
3. Next Generation Sequencing Technologies; Illumina 1G Analyzer, Roche 454 (Chip-seq, RNA-seq)
4. Bioinformatics support: assistance in experimental design and data analysis.

More detail on services offered is available at the following url: [http://derc.ucsd.edu/cores/transcriptional-genomics.shtml](http://derc.ucsd.edu/cores/transcriptional-genomics.shtml)

**Core Contacts:**

BIOGEM Core
Agilent and Illumina Arrays
Solexa Sequencing
James Sprague
(858) 822-4231
james@microarrays.ucsd.edu

GeneChip Core
Affymetrix and Nimblegen Arrays
454 Sequencing
Jorge Valencia
(858) 552-8585 x7100
genechip@vapop.ucsd.edu

Bioinformatics support: Roman Sasik, PhD. (858) 822-3283
sasik@corgon.ucsd.edu