Most Recent Publications by Center Members


New Grants by Center Members

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- Lu, Shelby. R01 AT01576, The role of SAMe in liver function and injury
- Mendler, Michel. R21 AA034269, RCT of SAMe in alcoholic liver disease
- Pandol, Steve. U54 AA0114643, Role of alcohol in pancreatic acinar cell death

Center Participates in NIAAA NRSA Trainee Workshop

By Rosy Macias
University of Southern California

The third biennial NRSA Trainee Workshop was held on November 22-23, 2003 in Indiana. The workshop on “Building a Foundation for Advances in Alcohol Research” was sponsored by NIAAA and the Indiana Alcohol Research Center and attended by our Center included Center Director, Hide Tsukamoto, Training Program Co-Director, Maria Runnegar, Postdoc Trainees, Taunia Lee, Derick Han and Mamatha Sadda, and Predoc Trainee Andy Melton.

The workshop is designed to showcase the work of trainees in NIAAA-supported alcohol research training programs. Taunia Lee presented her work on “Abnormal Hepatic Methionine and Glutathione Metabolism in Patients with Alcoholic Hepatitis,” and Andy Melton presented his work on “Fibrosis in Alcoholic Liver Disease: Regulation of Basal and Active Tension in Hepatic Stellate Cells” Poster presentations included Derick Han’s poster “Mitochondrial GSH Depletion by Ethanol: Effect on Superoxide and Hydrogen Peroxide Production by Mitochondria” and Mamatha Sadda’s on “S-Adenosylmethionine and Cell Death.”

This workshop focused on the work of our young scientists, and everyone that participated found the workshop to be stimulating and came back impressed with the diverse range of stellar research being conducted by the young scientists at all of the alcohol research centers.

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Center Members Participate in American Liver Foundation’s Annual Liver Walk

By Anne Taguchi
University of Southern California

As is our annual tradition, Center Members once again joined the American Liver Foundation’s Greater Los Angeles Chapter for their Annual Liver Walk at Griffith Park on May 31st. In addition to walking for a good cause, we enjoyed all the food, entertainment and activities; in addition to seeing our friends and getting out for a good walk.

The Center raised $500, and the event raised $84,000 for the American Liver Foundation!

We look forward to joining them again next year on June 5, 2004.
Spotlight on... Michel Mendler
By Maria Runnegar
University of Southern California

Michel is Assistant Professor of Clinical Medicine (Division of Gastrointestinal and Liver Diseases) at USC and a very active member of the Research Center for Alcoholic Liver and Pancreatic Diseases since his return to Los Angeles in 1999. Michel was born in San Francisco but came to LA shortly after. All his schooling was in San Monica. Michel and his parents lived next door to Neil Kaplowitz and one of the most vivid memories of his early childhood was of first meeting Neil and when Neil told him that he was a liver doctor, Michel's reaction was 'how boring.' Little did he know...

An undergraduate degree at UCLA with a major in Biochemistry followed. In 1985 Michel's family moved to Paris. Michel, who had always wanted to be a doctor was admitted to the Medical School in Rennes. Two summers spent in Los Angeles working in Neil Kaplowitz’s lab were critical for Michel's decision to aim towards a career in academic medicine. While a medical student in Rennes Michel earned his living by working as a translator of scientific papers. This was an opportunity for learning early on about different, more sophisticated aspects of medicine. This, combined with a very interesting rotation in GI-Hepatology led Michel to Internal Medicine and a fellowship in GI-Hepatology at the Dupuytren University Hospital in Limoges, France. Michel's very first research project in clinical medicine was to study and compare different imaging techniques for the diagnosis of fatty liver. A finding from this work was the association of fatty liver with iron overload. The opportunity to explore further this finding came with an appointment as junior staff back in Rennes at the Clinique des Maladies du Foie and INSERM Unité 49. A large proportion of the population of Bretagne is of Celtic origin and therefore genetically more prone to hemochromatosis. With the mentorship of renowned hepatologist Pierre Brisot, Michel developed his research and went to show that insulin resistance and fatty livers are associated with hepatic iron overload. That was 'where the real interest in NASH began.'

Although Michel was interested in translational and clinical problems he decided that he needed exposure to basic science. What followed was a one year accelerated Master in Molecular Biology looking at iron, insulin resistance in ob/ob mice. During this period Michel attended the AASLD meeting in Chicago where he met Pete Reynolds, Shelly Lu and Neil Kaplowitz again. He was encouraged to come and join the faculty of the Division of GI and Liver at USC in 1999. Working first at the Liver Unit at Rancho Los Amigos Medical Center and more recently at the USC Medical School Michel moved away from studies of iron overload to concentrate on fatty liver disease.

NAFLD (non-alcoholic fatty liver disease) is characterized by fat accumulation in the liver, in NASH (non-alcoholic steatohepatitis) the fat accumulation is combined with inflammation. The figure to the right sketches the various aspects of this of disease that Michel is interested in. Michel's work is focused on determining how steatosis influences the clinical course of different liver diseases: hepatitis C and alcoholic liver disease. Another major aspect of Michel's work is aimed at establishing a clinical database that includes history of the disease and tissue bank (biopsies and blood), which will facilitate the study of the development of fatty liver disease prospectively with great epidemiological value.

An objective scoring system for NASH was lacking. Michel together with Drs. Kahan and Rajan, pathologists, has established a novel histological system for NASH. This objective scoring system will lead to interesting correlations when validated and hopefully taken up by other groups working with fatty liver disease.

Michel is also working closely with Karen Lindsay on the relationship between hepatitis C and fatty liver disease. It has become clear that treatment for HCV cannot stand alone. Rather it is necessary to follow in diabetes, alcohol, obesity, and fatty liver disease as they all accelerate progression and decrease response rate in HCV.

Michel will shortly start a prospective random controlled, double blind study of the effect of S-adenosylhomocysteine (SAH) in mild alcoholic hepatitis. This study is in close collaboration with Shelly Lu. The question asked is whether SAH taken for one year can decrease the rate of progression and perhaps reverse some of the liver pathology. The special strength of this study is the combination of clinical and laboratory parameters that are going to be measured including markers of liver function, inflammation and methionine metabolism. This will lead to a better understanding of the pathophysiology of alcoholic liver disease and ultimately to new therapeutic drugs and regimens.

Finally, Michel and his wife Florence are the doting parents of enchanting two year old Roxanne and of two month old Axel Louis.

Continued on page 3

2003 Lee Summer Student Fellowship Awards
By Anne Taguchi
University of Southern California

In the summer of 2001, the Center instituted a program to promote involvement of undergraduate and Master's students in research on our Center's theme. The program is named after Dr. S.P. Lee who made a donation toward this noble cause. This program entails a minimum of 8 weeks of research during the summer in the Center investigator's laboratory and a required presentation on his/her research at the Center's Progress Report Meeting which was held on August 18, 2003.

This year, three students participated in our program. Kristy Sutton, undergraduate student at UCLA worked with Dr. Surayia Rashid on screening differentially regulated protein expression in activated hepatic stellate cells by proteomic technology. Julia Chen, graduate student at USC worked with Dr. E. Laird-Offringa on a project entitled, "Development of a tetracycline-inducible vector system for the analysis of Hu protein function." Each student that presented received a certificate and a $800 check upon completion of their fellowship. All in attendance were very impressed with the student's work and with the quality of their presentations. Congratulations to all!!

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![Student Kristy Sutton] (Left) with mentor, Sauraya Rashid, Ph.D. of USC.

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Left: Student Kristy Sutton with mentor, Sauraya Rashid, Ph.D. of USC.
Bottom: Student Yi Ching with mentor Li Laird-Offringa, Ph.D.

![Student, Julia Chen with mentor] (Left) Maria Runnegar, Ph.D. for mentor, Michael Lai, M.D. of USC.

![Student, Y Min Ji with mentor] (Right) Michael Lai, M.D. of USC.

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Today

Fall 2003

Featured Publication By Former Postdoctoral Fellow, Cheng Ji, Ph.D.

Alcohol + Homocysteine → Fatty Liver

ER Stress → C/EBPβ etc. → Apoptosis

Ca++ NFKB → Mitochondria → Inflammation


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