



SCIENCE FOR THE BENEFIT OF HUMANITY

Center for Clinical and Translational Science e-NEWSLETTER

Center News

Faculty and Clinical Scholars Honors and Activities

Dr. Ralph Steinman Wins Lasker Award, Rockefeller's 20th, and Chief Clinical Scholar, Edgar Charles Receives K08 Award!

Dr. Ralph Steinman was awarded the 2007 Albert Lasker Award for Basic Medical Research for his pioneering and landmark studies of dendritic cells. His discovery of the role of dendritic cells in antigen presentation has truly revolutionized our understanding of the immune response and opened up innumerable translational opportunities, including treatment of malignancies, enhancement of vaccine efficacy, and control of immune tolerance. The Lasker Award was presented to Dr. Steinman by Dr. Joseph Goldstein, Rockefeller Trustee, at a luncheon honoring the awardees in September, 2007.

Dr. Jan Breslow was the recipient of the 2005 New York City Mayor's Award for Excellence in Biological and Medical Sciences; he was also named 2006 Distinguished Scientist by the American Heart Association, and became a Distinguished Fellow of the International Atherosclerosis Society in 2007.

Dr. Elaine Fuchs was elected a Fellow of the AAAS in 2007-8 and was invited to give a series of 4 special lectures at the College de France, founded in 1533 in Paris, France.

Dr. Martin Markowitz delivered the Pioneers in Science Lecture, John Hopkins University School of Medicine, Baltimore, MD in May 2007. The title of his talk was "The Role of the GI Tract in the Pathogenesis of Acute HIV Infection."

Dr. Barry Coller was the keynote speaker at the Columbia University CTSA retreat held on January 10th, 2007. The title of his talk was "The Joys of Translational Research in the CTSA Era". He also delivered the 2007 C. Thomas Caskey Lecture at the University of South Carolina on October 22nd titled "Responsible Biomedical Science in the 21st Century: The Role of the Physician's Oath". On

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iRIS Rollout

Information Technology's iRIS software provides new features for Investigators

By Claudia Peisert and Donna Brassil

The Integrated Research Information System (iRIS) has been partially introduced over the last several months at the Rockefeller University Hospital. The nursing staff, clinical research coordinators, and other key users within the Hospital have collaborated with the Informatics Core in planning, configuring, and implementing iRIS for use in the Center for Clinical and Translational

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Rockefeller University Hospital Introduces New Nurse Manager of Inpatient Unit

By Melissa Offenhartz

Attracted by the challenges of research nursing, Veronica M. Whalen, BSN, MA, RN joined The Rockefeller University Hospital in January as the Nurse Manager of the Inpatient Unit. Veronica brings to Rockefeller a broad and deep background in all levels of healthcare delivery. She has practiced in three states and has strong regulatory

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Announcements

Special Symposium to Honor Dr. Mary Jeanne Kreek on May 16, 2008

Dr. Mary Jeanne Kreek will be honored with special symposium that will feature presentations from many distinguished alumni from her laboratory. President Paul Nurse will participate and Dr. Nora Volkow, Director of the National Institute on Drug Abuse at the National Institutes of Health, will deliver the keynote address. Dr. Jeffrey Friedman, Head of the Laboratory of Medical Genetics and Investigator, Howard Hughes Medical Institute will also participate. Please contact Mr. Brian Reed at reedb@rockefeller.edu for more information about this special event.

Seminars in Clinical Research

Wednesday, March 5, 2008

12:00 pm - 1:30 pm - 110B Nurses
Residence

*Dendritic Cell Subsets and Plasticity:
Implication in Human Diseases*

Yong Jun Liu, M.D., Ph.D., Vivian L. Smith Distinguished Chair in Immunology & Professor Director, Center for Cancer Immunology Research, The University of Texas, MD Anderson Cancer Center

Wednesday, March 19, 2008

12:00 pm - 1:30 pm - 110B Nurses
Residence

*Clinical Trials with Cell and Gene Therapy
for Melanoma Patients*

Mark Dudley, Ph.D., Head, Cell Production Facility, Surgery Branch, National Cancer Institute, National Institutes of Health

iRIS Rollout (continued from page 1)

Science. There are two key components of iRIS: Study Assistant and Review Board Assistant. Study Assistant implementation began in September 2007 and currently approximately 75% of the participants studied in the Outpatient Research Center have been integrated into iRIS' Study Assistant. This means that study personnel are able to electronically generate inclusion/exclusion criteria checklists, order sheets, and worksheets for each protocol-specific study visit, and schedule study participants with the assistance of a calendar generated for each participant. Visits are then recorded, along with the study-specific tasks and procedures, in the iRIS database, thus documenting these activities in a manner that meets all Good Clinical Practice (GCP) and audit requirements. The implementation of iRIS Study Assistant on the inpatient unit has just begun with a single protocol.

The second component of iRIS is the Review Board Assistant. This permits electronic production and distribution of protocols to both the Advisory Committee for Clinical and Translational Science (ACCTS) and the IRB in compliance with GCP. Documents can be signed electronically or by digital signature, the latest state of the art technique. Review Board Assistant will be launched in March with two ACCTS and IRB submissions handled by investigators and reviewers through the iRIS system. The full rollout will take approximately one year to complete as investigators and staff members receive individualized training in preparing and reviewing protocols in iRIS. Once this is completed, a large portion of the Annual Progress Reports to the IRB will be generated through iRIS' databases, including the number of screened, enrolled, and completed participants (including ethnicities and racial statistics) and adverse events. This system will not only save time but also insure consistency and accuracy in reporting data.

For further information contact Jean Jenkins (jean@rockefeller.edu), Ummei Johra (ujohra@rockefeller.edu), or Donna Brassil (dbrasil@rockefeller.edu)

Rockefeller University Hospital Introduces New Nurse Manager of Inpatient Unit

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from Villanova University. She is the proud mother of three college-aged children, including a pair of twins, and enjoys the activities of a large extended family. Veronica is happy to be a NYC resident and has been spending her free time navigating the New York City real estate market and working as a poll inspector for the NYC Board of Elections.

Howard Hang and David Allis Join the Faculty of the Center for Clinical and Translational Science

Dr. Howard Hang, Head of the Laboratory of Chemical Biology and Microbial Pathogenesis, and Dr. David Allis, Head of the Laboratory of Chromatin Biology and Epigenetics, have joined the faculty of the Center for Clinical and Translational Science. Dr. Hang's research interests include how posttranslational modifications of bacterial proteins affect virulence and how to identify small molecule inhibitors of pathways involved in posttranslational modifications. He is also interested in identifying bacterial peptides that can elicit a host immune response. His studies have important implications for vaccine development. He currently is collaborating with the Collier lab in the design of new small molecule antiplatelet agents. He joined Rockefeller from the Whitehead Institute for Biomedical Research at the Massachusetts Institute of Technology in 2007. Dr. Allis is internationally recognized for his pioneering studies of the covalent histone modifications that contribute to epigenetic control of chromatin structure and gene expression. His studies have profound implications for understanding a number of different diseases and provide insights into potential therapeutic targets. He is a member of the National Academy of Sciences and recipient of the 2007 Gardiner Foundation International Award.

Faculty and Clinical Scholars Honors and Activities (continued from page 1)

November 7, 2007 Dr. Collier delivered the Astute Clinician Lecture at the NIH Clinical Center. This lecture series was established by the Director of the NIH as part of the Director's Lecture Series. The title of his presentation was "From the Rivers of Babylon to the Coronary Blood Stream". Dr. Collier chaired the External Advisory Board review of the University of Pennsylvania CTSA on November 19, 2007. On December 13, 2007, he delivered the third in a series of webcasts in conjunction with the Clinical Directors Network (CDN), the Center's partner in its outreach efforts. The title of his presentation was "Anti-Platelet Therapy in a Community Care Setting".

Dr. Edgar Charles, Chief Clinical Scholar, was awarded a 5 year K08 Award to study Characterization of Clonal B Cell Populations in Individuals with Hepatitis C Infection. In addition, Dr. Charles's first authored paper "Clonal Expansion of Immunoglobulin M+CD27+ B Cells in HCV-associated Mixed Cryoglobulinemia" was published in *Blood* on February 1, 2008 (111:1344-1356). His coauthors were Rashidah M. Green, Svetlana Marukian, Andrew H. Talal, Gerond V. Lake-Bakaar, Ira M. Jacobson, Charles M. Rice, and Lynn B. Dustin.

Dr. Knut Wittkowski is currently serving as President Elect of the Association of GCRC Statisticians and is scheduled to become President in 2010. The Association is currently exploring its transition to reflect a focus on the new CTSA program. Dr. Wittkowski has recently given presentations on "Bioinformatics Tools Enabling U-Statistics: From Sports to Microarrays" to the Department of Biostatistics at Vanderbilt University Medical Center, and the Department of Statistics at the College of Arts & Sciences, University of Kentucky.

Grant Year 2 Pilot Project Awards Announced

Rockefeller University CCCTS is pleased to announce its Grant Year 2 Pilot Project Awards.

Study Title: Preclinical characterization of the immunity induced by a DEC205-HIV gag fusion vaccine.

Name of PI: Marina Caskey, MD (Clinical Scholar)

Brief Study Description: This pilot study aims to characterize the magnitude and the quality of the immune response of prime-boost immunization with DEC-205-p24 plus poly IC in comparison to other standard immunizations. By omitting the use of anti-CD40 together with poly IC, the adjuvant will be more feasible to use in volunteers, and to compare poly I:C12U (Ampligen) to poly IC as an adjuvant in DEC-205-p24 prime-boost immunization and select the optimal dose and route of administration. By moving to Ampligen from its analogue, poly IC, we will be using an adjuvant that has previously been administered at high doses to large numbers of humans with no serious adverse events.

Funding Amount: \$25,000

Study Title: Projects HITS-NY

Name of PI: Delivette Castor (Clinical Scholar)

Brief Study Description: This pilot project is an observational pilot study to describe how sexual and drug-using network factors influence HIV-1 risk among MSM. This study will also explore the relation between individual drug use / sexual behavior and social network factors that influence risk of HIV-1 infection and transmitted drug resistance (TDR). The investigator intends to recruit 280 MSM who are seeking an HIV-1 screen at the Rockefeller University ADARC clinic, and capture demographic, socioeconomic characteristics, psychosocial and mental health assessments, sexual- and drug using behaviors, and knowledge, awareness and use of prophylactic antiviral therapy at baseline. Furthermore, the investigator intends to follow those who are recently / acutely HIV-1 infected for two years after diagnosis to examine the dynamic nature of these factors.

Funding Amount: \$25,000

Study Title: Study of the B-cell Tolerance Checkpoints in Pemphigus Vulgaris

Name of PI: Mouquet Hugo

Brief Study Description: Pemphigus vulgaris (PV) is a life-threatening organ-specific autoimmune disease affecting skin and mucosa. the goal of this pilot project is to enumerate autoreactive and polyreactive B cells in different B cell compartments in 4 new diagnosed PV patients using the single cell cloning and antibody expression approach previously developed to study the B cell tolerance in healthy subjects and SLE patients. The investigator anticipates that these experiments will establish a relationship between repertoire, auto- and polyreactivity, and a B cell tolerance breakdown in PV patients allowing thus, a better understanding of the disease etiology

Funding Amount: \$25,000

Study Title: Elucidation of the neuroendocrine effects of disulfiram in rats in the setting of chronic “binge” cocaine administration and acute cocaine withdrawal

Name of PI: Igor Kravets, MD (Clinical Scholar)

Brief Study Description: The goal of the proposed project is to determine whether disulfiram, a promising pharmacological agent for the treatment of cocaine abuse, derives part of its effect from an ability to alter stress responsivity of the hypothalamic-pituitary-adrenal (HPA) axis as well as the amygdalar stress response system and to influence hormones involved

New Publications from the CCTS

From tumor immunity to psoriasis; from novel HIV therapy to stress and substance abuse; and from β -amyloid and autophagy to platelet adhesion, members of the CCTS are providing new molecular data with profound implications for understanding, treating, and preventing human disease.

Santomasso BD, Roberts WK, Thomas A, Williams T, Blachère NE, Dudley ME, Houghton AN, Posner JB, Darnell RB. A T-cell receptor associated with naturally occurring human tumor immunity. *Proc Natl Acad Sci U S A.* 104:19073-19078, 2007.

Zaba LC, Cardinale I, Gilleaudeau P, Sullivan-Whalen M, Suárez Fariñas M, Fuentes-Duculan J, Novitskaya I, Khatcherian A, Bluth MJ, Lowes MA, Krueger JG. Amelioration of epidermal hyperplasia by TNF inhibition is associated with reduced Th17 responses. *J Exp Med.* 204:3183-3194, 2007.

Quaia E, D’Onofrio M, Cabassa P, Vecchiato F, Caffarri S, Pittiani F, Wittkowski KM, Cova MA. Diagnostic value of hepatocellular nodule vascularity after microbubble injection for characterizing malignancy in patients with cirrhosis. *AJR Am J Roentgenol.* 189:1474-1483, 2007.

Berwick M, Satagopan JM, Ben-Porat L, Carlson A, Mah K, Henry R, Diotti R, Milton K, Pujara K, Landers T, Dev Batish S, Morales J, Schindler D, Hanenberg H, Hromas R, Levran O, Auerbach AD. Genetic heterogeneity among Fanconi anemia heterozygotes and risk of cancer. *Cancer Res.* 67:9591-9596, 2007.

Sullivan-Whalen M, Gilleaudeau P. Psoriasis: hope for the future. *Nurs Clin North Am.* 42:467-484, 2007.

Zaba LC, Fuentes-Duculan J, Steinman RM, Krueger JG, Lowes MA. Normal human dermis contains distinct populations of CD11c+BDCA-1+ dendritic cells and CD163+FXIIIa+ macrophages. *J Clin Invest.* 117:2517-2525, 2007.

Mehandru S, Vcelar B, Wrin T, Stiegler G, Joos B, Mohri H, Boden D, Galovich J, Tenner-Racz K, Racz P, Carrington M, Petropoulos C, Katinger H, Markowitz M. Adjunctive passive immunotherapy in human immunodeficiency virus type 1-infected individuals treated with antiviral therapy

Grant Year 2 Pilot Project Awards Announced

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in stress response.

Funding Amount: \$25,000

Study Title: Dietary Interventions for Insulin Resistance and the Metabolic Syndrome

Name of PI: Lisa Neff, MD (Clinical Scholar)

Brief Study Description: This pilot study will test the following hypotheses: 1) In individuals with insulin resistance and the metabolic syndrome, the Dietary Approaches to Stop Hypertension study diet (the DASH diet) and the low glycemic index diet (low GI diet) will improve insulin sensitivity (as measured using the hyperinsulinemic euglycemic clamp) to a greater extent than the average American diet; and 2) Weight loss will enhance the insulin-sensitizing effects of the DASH diet and the low GI diet.

Funding Amount: \$25,000

Study Title: Obesity associated colorectal inflammation, the effects of weight loss

Name of PI: Swaroop Pendyala, MD (Clinical Scholar)

Brief Study Description: The pilot project will test the hypothesis: Does significant weight loss achieved with dietary modifications decrease chronic inflammation in colorectal epithelium and reduce fecal calprotectin levels? Inflammation of the colorectal mucosa will be documented by studying rectal biopsies done through proctosigmoidoscopy. These biopsies will be evaluated for mucosal inflammation by immunohistochemistry, cytokine concentrations and gene microarray studies. In addition, fecal calprotectin, a marker of intestinal inflammation, will be measured before and after weight loss. Studying the changes in colorectal inflammation with weight loss in obesity will be an initial step towards understanding the pathogenesis of colon cancer. The investigator anticipates that the data generated from this study will allow us to plan for further interventional studies aimed at reducing colonic inflammation and colon cancer. **Funding Amount:** \$25,000

Study Title: Generation of patient-specific hepatocytes for the analysis of genetic determinants of susceptibility to Hepatitis C virus infection

Name of PI: Alexander Ploss, PhD (Rice Laboratory)

Brief Study Description: The pilot project proposes to generate patient-specific human hepatocytes as a renewable source for primary liver tissue and to dissect host genetic determinants of HCV infection.

Funding Amount: \$25,000

Study Title: Epstein Barr Virus Infected B Cell and Humoral Autoimmunity in Multiple Sclerosis

Name of PI: Jan D. Lünemann, MD

Brief Study Description: Large prospective epidemiological studies indicate that patients with MS, including children with MS, are universally infected with Epstein-Barr Virus (EBV) and that the risk of developing MS is increased in individuals with a history of infectious mononucleosis (IM) and elevated titers of EBV-specific antibodies. The mechanisms responsible for this association are not understood. In previous experiments the investigator found that patients with MS show a qualitatively and quantitatively distinct EBV nuclear antigen 1 (EBNA1)-specific CD4+ T cell repertoire compared to HLA-DR matched healthy virus carriers (3). Here, the investigator hypothesizes that host-EBV interactions are dysregulated at the level of infected B cells in MS patients, which potentially triggers aberrant cellular and humoral EBV-specific immune responses, and that EBV assists in the survival of pathogenetically relevant autoreactive B cell species.

Funding Amount: \$25,000

New Publications from the CCTS

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during acute and early infection. *J Virol.* 1:11016-11031, 2007.

Koob G, Kreek MJ. Stress, dysregulation of drug reward pathways, and the transition to drug dependence. *Am J Psychiatry.* 164:1149-1159, 2007.

Williams TJ, LaForge KS, Gordon D, Bart G, Kellogg S, Ott J, Kreek MJ. Prodynorphin gene promoter repeat associated with cocaine/alcohol codependence. *Addict Biol.* 12:496-502, 2007.

Guttman-Yassky E, Lowes MA, Fuentes-Duculan J, Whynot J, Novitskaya I, Cardinale I, Haider A, Khatcherian A, Carucci JA, Bergman R, Krueger JG. Major differences in inflammatory dendritic cells and their products distinguish atopic dermatitis from psoriasis. *J Allergy Clin Immunol.* 119:1210-1217, 2007.

Lünemann JD, Schmidt J, Schmid D, Barthel K, Wrede A, Dalakas MC, Münz C. Beta-amyloid is a substrate of autophagy in sporadic inclusion body myositis. *Ann Neurol.* 61:476-483, 2007.

Jirousková M, Jaiswal JK, Collier BS. Ligand density dramatically affects integrin alpha IIb beta 3-mediated platelet signaling and spreading. *Blood.* 109:5260-5269, 2007.

Mitchell WB, Li J, Murcia M, Valentin N, Newman PJ, Collier BS. Mapping early conformational changes in alphaIIb and beta3 during biogenesis reveals a potential mechanism for alphaIIbbeta3 adopting its bent conformation. *Blood.* 109:3725-3732, 2007.