



Center for Clinical and Translational Science e-NEWSLETTER

Center News

Inaugural Clinical and Translational Research Day

By Michelle Romanick

The Inaugural Clinical and Translational Research Day was held in Caspary Auditorium at The Rockefeller University on Thursday, September 20, 2012. The program highlighted translational medicine research progress at Rockefeller and focused on research being conducted by investigators and trainees. The event, which was co-organized by Dr. Neil Renwick and Michelle Romanick, was designed to enhance collaborations between members of different Rockefeller laboratories and other investigators in the area.

In fact, the program attracted participants from Columbia University Medical Center, Memorial Sloan-Kettering Cancer Center, Mount Sinai School of Medicine, New York-Presbyterian Hospital/Weill-Cornell Medical Center, and Yale University. Virtual attendees from across the United States, as well as from Israel, Saudi Arabia, and United Kingdom viewed the event via a webcast conducted through the Clinical Directors Network, Inc.

The opening presentations were devoted to the past, current, and future of translational research at The Rockefeller University Hospital. Dr. Jules Hirsch, Professor Emeritus, spoke about "The Rockefeller University Hospital and the Translational Research Enterprise," highlighting the historical roles that Rockefeller University and the Rockefeller University Hospital, respectively, played as the country's first institute and hospital devoted exclusively to biomedical and clinical research. Dr. Hirsch shared his own experiences at Rockefeller University since 1954, emphasizing that while the technologies for conducting research have changed, the mission of Rockefeller University has remained the same.

Dr. James Krueger, Chief Executive Officer of the Hospital, presented "Along a 100-year Path of Bedside-to-Bench Translation: Updating Pathways of Pathogenic Inflammation in Psoriasis" in which he delineated the steps from a diagnosis to current research in advancing the treatment of this disease.

Dr. Barry Collier, Physician-in-Chief of the Hospital, addressed the future of translational research with his presentation entitled "Bringing Science to the Clinical Investigation Process." Dr. Collier highlighted how the Center for Clinical and Translational Science is using data to speed the development of the higher quality research protocols (Navigation Program), recruit individuals into research studies, and learn about research participants' perceptions of their research experience.



Dr. John I. Gallin, Director of the NIH Clinical Center
Keynote Speaker

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The Rockefeller University Center for Basic and Translational Research on Disorders of the Digestive System hosts its first annual symposium and research in progress poster session

By Maija Neville-Williams

The Rockefeller University Center for Basic and Translational Research on Disorders of the Digestive Systems (CDDS) hosted its first symposium and research in progress poster session on October 22, 2012, attracting basic and translational scientists from the Rockefeller campus and neighboring institutions. Sponsored by the Leona and Harry B. Helmsley Charitable Trust, the symposium focused on emerging developments in digestive disease research and included research talks from Martin Blaser, M.D. of New York

University School of Medicine on the "Effects of Early Life Antibiotics on Developmental Phenotypes"; Balfour Sartor M.D. of University of North Carolina at Chapel Hill on "Host-microbial Interactions in Chronic Intestinal Inflammation: Implication for IBD Pathogenesis and Treatment"; Leonard Saltz, M.D. of Memorial Sloan-Kettering Cancer Center on "One Giant Leap for a Man (or Woman); One Small Step for Mankind: Curing Rectal Cancer, One Individual at a Time"; Peter R. Holt, M.D. from Rockefeller on "Obesity and Cancer Translational

Studies at the Rockefeller University", and Charles M. Rice, Ph.D. from Rockefeller on "Model Systems for the Study of Hepatotropic Pathogens and Liver Disease".

Investigators updated the audience on the latest advances research in inflammatory bowel disease, obesity, cancer, liver disease, and hepatitis. The symposium concluded with a research in progress poster session, including both senior and junior investigators from Rockefeller and Weill-Cornell.

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38 New Pilot Awards Funded by the Center for Clinical and Translational Science

By Michelle Romanick

The Rockefeller University Center for Clinical and Translational Science (CCTS) and the Center for Basic and Translational Research on Disorders of the Digestive System (CDDS) awarded 38 pilot projects this year (20 CCTS and 18 CDDS). Ten recipients are CCTS Clinical Scholars and 2 are to Rockefeller Early Phase Physician Scientists (REPPS). A total of 47 applications were submitted, representing the highest number received to date. CCTS committed \$392,000, CDDS committed \$312,500, and \$25,000 was provided by the Katerina and Andreas C. Dracopoulos Family Science and Society Initiative at The Rockefeller University, for a total commitment of \$729,500. This brings the grand total of pilot project funding to \$2,014,434 since this program was begun under the initial CTSA grant in 2006.

Pilots Projects Led by CCTS Clinical Scholars

1. **Nathalie Burg, MD** (Coller Lab): *Proposal to discover and produce antibodies to latent transforming growth factor- β 1 to elucidate mechanisms and improve the therapy of Systemic Sclerosis.* This project will test the hypothesis that autoantibodies and/or enhanced shear stress in SSc microvasculature facilitates thiol-disulfide exchange and ongoing TGF- β 1 activation. It will also provide insights into the mechanism of shear-induced TGF- β 1 activation by developing mAbs that inhibit the activation and by mutating the CXXC motifs in LTBP-1, which are candidates for mediating thiol-disulfide exchange.
2. **Louis Cohen, MD** (Brady Lab): *Metagenomic analysis of bacterial natural products and their role in the intestinal microbiome.* This project will establish an in-vitro infection system based on hepatocyte-like inducible pluripotent stem cells (iHLCs), which have been previously shown to support hepatitis C virus infection. Those cells will be infected with either a pseudo typed virus expressing a reporter gene or by a wild-type virus derived from HBV producing cell line or from infected patients' sera. The potential to dissect the differentiation stage at which the iHLCs become permissive to HBV infection, and the ability to generate iHLCs from stem cells of individuals harboring different genetic backgrounds will enable us to address key questions such as host factors essential for HBV infection and the importance of certain genetic backgrounds in directing the natural history of HBV infection.
3. **Thalia Parazi, MD, PhD** (Tuschl Lab): *Development of multicolor fluorescence RNA in situ-hybridization assays for breast cancer diagnosis and prognosis.* This project will to develop a multicolor fluorescence RNA in situ hybridization (ISH) approach, by which gene and non-coding RNA (ncRNA) expression can be visualized at single-cell resolution along with histological parameters to enhance the accuracy of breast cancer diagnosis for three known breast cancer markers; at the same time we aim to identify ncRNAs that may serve as reference controls or comprise diagnostic and prognostic markers.
4. **Daniel Gareau, PhD** (Krueger Lab): *The Melanoma Advanced Imaging Dermatoscope.* This project will create the hardware and software to expand the spectral range of the mAID from the UV (300nm) to the IR (1600nm). The overall goal is to better identify spectral ranges of diagnostic value toward a comprehensive, automated imaging system as a clinical and research tool. Re-engineering the currently used dermatoscope from a conventional red/green/blue (RGB) camera, to one that images pigmented lesions across a wide spectral range beyond RGB, we would like to create an overall package that is relatively inexpensive and could be adopted in general dermatology practice.
5. **Sharon Karmon, MD** (Ho/Markowitz Lab): *Mediators of immune activation and senescence in HIV-1 infected subjects.* This project will explore the effects of starting cART during acute, early or chronic infection on markers of inflammation and immune senescence, as preliminary data has supported the hypothesis that very early use of antiretroviral therapy correlates with normalization of markers.
6. **Florian Klein, MD** (Nussenzweig Lab): *Improvement of HIV-therapy by a combination of anti-retroviral medication and broad neutralizing antibodies in humanized mice.* This project will investigate the potential improvement in HIV-therapy by combining classical/anti-retroviral therapy with the new antibody treatment modality in HIV-1-infected humanized-mice.
7. **Xiao-Fei King, MD, PhD** (Cassanova Lab): *Genetic and immunological dissection of the pathogenesis of chronic mucocutaneous disease in patients with Down Syndrome.* Down syndrome (DS) patients may have enhanced responses to interferons (IFNs) due to an extra chromosome 21, and may also suffer from an impaired immunity mediated by IL-17 T cells, which could explain the fungal infections and provide a new avenue for treatment. This project will investigate DS patients' IFN responses and IL-17 immunity.
8. **Ana Pereria, MD** (McEwen Lab): *Sleep Disordered Breathing and Glutamate-Induced Excitotoxicity in the Human Hippocampus as a Risk for Alzheimer's disease.* This project will study potential mechanisms through which Sleep-Disordered Breathing (SDB) may increase the risk of Alzheimer's Disease (AD) by investigating the phenomenon of glutamate-mediated excitotoxicity and with measures of the pathological hallmarks of AD, hyper phosphorylated tau and A β 42.
9. **Uri Sela, MD, PhD** (Fischetti Lab): *A novel approach to induce a protective immune response to a vaccine against Staphylococcus aureus.* This project will induce T cell immunity by using a novel approach of dendritic cell (DC) targeting that was developed here at the Rockefeller University by the Ralph Steinman laboratory and is currently in clinical trials for an HIV vaccine. The novel vaccine approach in this pilot project will be tested for its protective capacity in a mouse model of S. aureus infection.

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New Clinical Scholars Join the Center for Clinical and Translational Science (CCTS)

By Michelle Romanick

On July 1, 2012, six new Clinical Scholars joined the Rockefeller University Clinical Scholars Program. They are: Drs. Nathalie Burg, Louis Cohen, Peter Forgacs, Xiao-Fei Kong, Uri Sela, and Amir Shlomai. Additionally, with support from the CCTS, Nikhil Dhingra joined the Krueger Laboratory as this year's medical student trainee in Clinical and Translational Science. Below are brief biographies and research interests of the new Scholars and medical student. Please join us in welcoming them.



Nathalie Burg, MD
nburg@rockefeller.edu
Mentor: Dr. Barry Collier

Dr. Nathalie Burg received her MD from New York University of Medicine. She completed her Internal Medicine Residency at the Mount Sinai Medical Center, and her Rheumatology Fellowship at New York University Medical Center. As a Clinical Scholar in Dr. Collier's lab, Dr. Burg will be studying the role of the protein LTBP-1 in shear induced transforming growth factor beta1 activation and will work on projects to discover and produce antibodies to latent TGF- β 1 to elucidate the pathologic mechanisms that cause systemic sclerosis and the related disorder scleroderma.



Louis Cohen, MD
lcohen@rockefeller.edu
Mentor: Dr. Sean Brady

Dr. Louis Cohen received his MD from Tufts School of Medicine. He completed his Internal Medicine Residency at Massachusetts General Hospital, and his Gastroenterology Fellowship at Mount Sinai Medical Center. As a Clinical Scholar in Dr. Brady's lab, Dr. Cohen will be studying metagenomic analysis of natural product pathways as they relate to inflammatory bowel disease.



Peter Forgacs, MD
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Mentors: Drs. Donald Pfaff and Nicholas Schiff

Dr. Peter B. Forgacs received his MD from the University of Szeged in Hungary. He completed his Medicine Internship and Neurology Residency at the New York-Presbyterian Hospital, Weill Cornell Medical Center and his Clinical Neurophysiology/Epilepsy Fellowship at Brigham and Women's Hospital, Harvard Medical School. As a Clinical Scholar in Drs. Pfaff's and Schiff's labs, Dr. Forgacs will be designing and developing a study involving assessment of the recovery of behavior and cognitive brain functions using multimodal imaging and quantitative EEG analysis in patients with disorders of consciousness.



Xiao-Fei Kong, MD, PhD
xiko262@rockefeller.edu
Mentors: Dr. Jean-Laurent Casanova

Dr. Xiao-Fei Kong received his MD from the Yangzhou University in China, and his PhD from the Université Pierre et Marie Curie in Paris, France. He completed his Residency in internal medicine at Ruijin Hospital, Shanghai Jiaotong University, School of Medicine in China. As a Clinical Scholar in Dr. Casanova's lab, Dr. Kong will be characterizing the genedosage effects to understand the clinical and immunological features of Down syndrome

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New Clinical Scholars Join the Center for Clinical and Translational Science (CCTS) continued from page 3



Uri Sela, MD, PhD
usela@rockefeller.edu
Mentor: Dr. Vincent Fischetti

Dr. Uri Sela received his MD from Tel Aviv University, and his PhD from the Weizmann Institute of Science in Israel. He completed his Internal Medicine residency at Tel Aviv University. As a Clinical Scholar in Dr. Fischetti's lab, Dr. Sela will be developing a group A streptococcal vaccine and studying the immunological properties of *Staphylococcus aureus* infections.



Amir Shlomai, MD, PhD
ashlomai@rockefeller.edu
Mentor: Dr. Charles Rice

Dr. Amir Shlomai received his MD from Hebrew University, and his PhD from the Weizmann Institute of Science in Israel. He completed his Internal Medicine residency, and his Gastroenterology and Liver Disease fellowship at Tel-Aviv Sourasky Medical Center. As a Clinical Scholar in Dr. Rice's lab, Dr. Shlomai will be working on multiple projects that aim to better understand the pathogenesis and virus-host interactions of hepatitis B and hepatitis C viruses, two pathogens that cause severe liver damage and liver cancer.



Nikhil Dhingra
nikdhing@gmail.com
Mentor: Dr. James Krueger

Mr. Nikhil Dhingra is currently a third year medical student at Columbia University College of Physicians and Surgeons. Mr. Dhingra is assisting on a number of projects that focused on the immunological aspects of inflammatory cutaneous diseases, with particular focus on atopic and contact dermatitis.

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10. **Amir Shlomai, MD, PhD** (Rice Lab): *Identifying essential host factors in hepatitis B virus life cycle by modeling infection in hepatocyte-like inducible pluripotent stem cells (iHLCs)*. This project will establish an *in-vitro* infection system based on hepatocyte-like inducible pluripotent stem cells (iHLCs), which have been previously shown to support hepatitis C virus infection. Those cells will be infected with either a pseudo typed virus expressing a reporter gene or by a wild-type virus derived from HBV producing cell line or from infected patients' sera. The potential to dissect the differentiation stage at which the iHLCs become permissive to HBV infection, and the ability to generate iHLCs from stem cells of individuals harboring different genetic backgrounds will enable us to address key questions such as host factors essential for HBV infection and the importance of certain genetic backgrounds in directing the natural history of HBV infection.

Pilots Projects Led by REPPS

1. **Jennifer Belasco, MD** (Krueger Lab): *Characterization of Inflammatory Pathways in Psoriatic Arthritis*. Preliminary data shows that while the skin disease of psoriatic arthritis (PsA) is histologically similar to the skin disease of psoriasis vulgaris (PsV), the specific immune activation in the PsV lesional skin may be different than the PsA lesional skin. In this study, the gene expression patterns of lesional and non-lesional skin biopsies from subjects with PsA and PsV will be examined by gene array analysis and the connection between skin and joint symptoms will be further explored.

2. **Manish Ponda, MD** (Breslow Lab): *The Effect of Oral Vitamin D vs. Ultraviolet Light on Cholesterol*. A randomized, placebo-controlled trial was conducted to test the effect of oral vitamin D repletion on cholesterol. Oral vitamin D therapy failed to improve the lipid profile, and thus did not translate into the inferred benefit derived from epidemiologic studies. A plausible explanation for the uncoupling of epidemiologic and intervention-based data for vitamin D therapy and cholesterol may be due to the route of vitamin D administration. Therefore, we propose testing the effect of oral, exogenous vitamin D as compared to ultraviolet light-induced, endogenous vitamin D on the lipid profile.

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Dr. Charles Rice's presentation, "Hepatitis C: Is the End in Sight?" focused on the challenges of diagnosing and treating hepatitis C virus with the goals of improving the lives of millions of infected individuals and eradicating the disease. Dr. Jean-Laurent Casanova's presentation, "From Childhood Infectious Diseases to Inborn Errors of Immunity" described how his lab has identified the genetic basis to explain why certain children develop severe clinical infections whereas others remain unharmed despite identical exposure.

The poster session was a highlight of the day, with 24 posters from, Clinical Scholars, members of the Rockefeller Early Phase Physician Scientists, and other investigators.

The Keynote speaker, Dr. John I. Gallin, Director of the NIH Clinical Center presented on "The Importance of Rare Diseases in Translational Research." Dr. Gallin focused on the rare hereditary immune disorder, chronic granulomatous disease (CGD). His laboratory described the genetic basis for several forms of CGD and has performed pioneering research on therapies to reduce life-threatening

bacterial and fungal infections in CGD patients. He emphasized that studies of rare diseases can be highly informative and useful for identifying molecular targets for treating common diseases. He also extended an invitation to the audience to apply for the new NIH grant "Opportunities for Collaborative Research at the NIH Clinical Center," to support collaborative research projects aligned with NIH efforts to enhance the translation of basic biological discoveries into clinical applications that improve health.

The last session of the Research Day included a presentation from Dr. Nina Papvasiliou, entitled "Co-opting a Host-Pathogen Interface for Therapeutic Purposes" in which she described her fascinating studies on trypanosomes.

Drs. Alexander Tomasz and Jonathan Tobin jointly presented on "Translational Microbe Hunters: Tracking MRSA in the New York Community". They described how their collaboration spanned from community-based diagnosis and treatment to molecular characterization of the microbe at the DNA level.

Judging from the active engagement of many participants in discussions throughout the day and the written evaluations at the end of the day, the inaugural Clinical and Translational Research Day was considered a great success.



Dr. Charles Rice



Dr. Jules Hirsch



Dr. Barry Coller



Dr. Jean-Laurent Casanova



Dr. Jonathan Tobin



Dr. Nina Papvasiliou



Dr. James Krueger



Dr. Alexander Tomasz

Meet the Scholar: Florian Klein, MD

By Michelle Romanick



Florian Klein, MD,

Dr. Florian Klein joined the Clinical Scholars Program at Rockefeller University in 2011 and was selected as Chief Clinical Scholar in 2012. Dr. Klein received his MD from the University of Cologne in Germany, and joined Dr. Michel Nussenzweig's Laboratory of Molecular Immunology in 2009 as a post-doctoral fellow after completing his residency in Internal Medicine at the University of Cologne.

Dr. Klein is currently investigating the antibody response to HIV-1 infection. Over the last years the Nussenzweig laboratory has been able to isolate and characterize antibodies that are highly potent in effectively neutralizing HIV-1. Based on those findings, Dr. Klein and his colleagues have recently demonstrated that a combination of these neutralizing antibodies are able to successfully treat HIV-1 infection in humanized mice. These promising results further encouraged the researchers to evaluate these antibodies in HIV-1 infected patients and human clinical trials are already planned.

Dr. Klein's interest in science and research extends to his pre-medical school years, but his first basic research experiences occurred in 2001 in the laboratory of Dr. Markus Mutschen during medical school. In Dr. Mutschen's lab, he focused on normal B cell development and on the transformation of B cells into leukemic B cells. This experience stimulated his

interest in B lymphocytes and antibodies, which led him to Dr. Nussenzweig's research and ultimately to joining his lab.

When asked about his experience in the Clinical Scholars Program, Dr. Klein said, "It is an outstanding program tailored to physicians and scientists that have strong interest in patient care and clinical or basic research. The program provides you with the knowledge and tools to pursue patient-orientated research, and it certainly exceeded my expectations. In my opinion, the key element of the program is the excellent weekly tutorial in which we discuss with Dr. Collier or Dr. Schlesinger different aspects related to translational research. Here, interesting perspectives develop and the discussions are always insightful. Finally, the Clinical Scholar Program allows you to work with exceptional people at the Rockefeller University and the Rockefeller Hospital. You benefit from their great experiences and expertise, which in turn, helps you to find your way in becoming a successful and responsible physician scientist. "

Clinical Scholars Visit Ellis Island

By Michelle Romanick

The Clinical Scholars visited Ellis Island on September 27, 2012 to take a step back into time to hear about the medical screening process of immigrants. In preparation for the visit, the Scholars read about how the American Eugenics Movement influenced the medical evaluations at Ellis Island and the 1924 legislation that severely limited immigration from Eastern European countries.

Mr. Thomas Bernardin, a licensed tour guide, provided important historical information on American Immigration. 20 Million immigrants passed through Ellis Island before its closing in 1954. Immigrants had to pass what was known as the "six second medical exam" before they were allowed to enter New York. The exam began as soon as the immigrants walked up the stairs from the first floor to the second floor. The doctors watched as the immigrants climb the stairs, looking for trouble walking, weakness, heavy breathing, or signs of impaired mental health. Each person's hair, face, neck and hands were rapidly examined. If an impairment was noted, the doctor wrote a letter in chalk on the individual's clothing



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indicating further examination was needed. About 2 of 10 persons received one or more letter: "L"= Lameness, "PG" = pregnant, "X"= possible mental illness and "FI"= further investigation was needed. Depending on the letter designation, immigrants were either denied entrance or sent to the hospital on Ellis Island, a complex of 15 medical buildings located across the ferry dock from the main building. Patients received high quality care and many were able to enter the country after their illness was treated.

Lynda Olender, New Director of Nursing and Patient Care Services



Lynda Olender joins Rockefeller University Hospital as the Director of Nursing and Patient Care Services this Fall, 2012. As a distinguished nurse leader, she brings over 40 years of experience from a variety of settings, including her previous role as an international consultant, her 10-year experience as a Chief Nursing Officer, as an Assistant Professor of Nursing at New York University, and in her most previous role as an Executive Consultant and Nurse Researcher at the James J. Peters VAMC. In her latter role she served as Co-Principal Investigator of an AONE seed grant-awarded study looking at the impact of a professional practice model with shared governance (PPMSG) on caring, work engagement and work empowerment in interdisciplinary staff within a tertiary inpatient VA healthcare setting.

Ms. Olender received her original nursing training at Kings County Hospital School of Nursing, her Baccalaureate Degree in Nursing from the College of Staten Island, her Master's Degree in Nursing Administration at New York University, her Post Masters's Certificate as an Adult Nurse Practitioner at Adelphi, and is currently completing her Ph.D in Nursing at Seton Hall University. Attesting to the merit of her doctoral work, she is the recipient of a Sigma Theta Tau grant to support her dissertation designed to examine the relationship between nurse manager caring and workplace bullying in nursing.

Throughout her career, Ms. Olender has studied academic and clinical nursing workplace incivility and bullying among peers and faculty. To that end, she has authored numerous publications and book chapters to create awareness of its prevalence and insidious nature, as well as making recommendations for the minimization and/or eradication of disruptive behavior in these settings. She has presented this work to a variety of audiences. She brings her passion for creating a culture of regard, both to academic and clinical venues and specifically, to Rockefeller University Hospital.

Ms. Olender is active within her profession and her local community as well. Currently, she serves as the Treasurer for the Greater New York Organization for Nurse Executives, has served two terms as Chair of the New York State Nursing Association's Council of Continuing Education, and is active within her church affiliation.

Here at Rockefeller University Hospital, in addition to her role as Director of Nursing and Patient Care Services, she also serves as Director of the Heilbrunn Family Center for Research Nursing. In this capacity, she is building upon the accomplishments of her previous predecessors and the advice of the distinguished External Advisory Board to enhance the role of the Clinical Research Nurse and to foster professional collaboration between Clinical Research Nurses and nurse investigators at Rockefeller University Hospital. Academic offerings include seminars and workshops to enhance the engagement of, and generate innovation among research nurses. In collaboration with Women & Science, Rockefeller University Hospital will once again host the Annual Beatrice Renfield Lectureship in Research Nursing on February 26, 2013.

Her work will also include enhancing the standards for the specialty practice of research nursing, the development of related education and training resources, and in collaboration with the International Association of Clinical Research Nursing (IACRN) nurse leaders at both national and international level, the development of a research agenda for Clinical Research Nurses.

We welcome Ms. Olender to our academic and clinical community!

The Rockefeller University Center for Basic and Translational Research on Disorders of the Digestive System hosts its first annual symposium and research in progress poster session

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Twenty-one posters were presented, including a poster by The Rockefeller University Hospital's Bionutrition department highlighting its support of metabolic studies and resources available to investigators who are interested in conducted research at the institution.

After the symposium was concluded, Dr. Martin Blaser led the first CDDS External

Advisory Board meeting. Attendees included other members of the Advisory Board, Drs. David Alpers, Barry Collier, Leonard Saltz, and R. Balfour Sartor, as well as members of the CDDS Executive Committee.

CDDS was established in 2012 with a \$15 million grant from the Leona M. and Harry B. Helmsley Charitable Trust to fund research in digestive disorders,

including metabolic diseases, cancers and infections. The Center supports interdisciplinary basic research and fosters collaborations among some 20 Rockefeller labs that study biological processes related to the digestive system. For more information please visit the CDDS website at <http://digestivedisorders.rockefeller.edu>.

Nutritional Pharmacology: Regulation of Drug and Hormone Metabolism by Components of the Human Diet

By Elizabeth (Betsy) Hanson



Kappas, Attallah
Courtesy of the Rockefeller Archive Center

Proteins, carbohydrates, and fats in foods can affect the manner and rapidity with which the body—principally the liver—processes and biotransforms drugs, and thus alters the drugs' effectiveness. In 1976, Attallah Kappas (1926-) and colleagues at the Rockefeller Hospital began a series of exacting metabolic studies in humans that first defined the specific effects of diet components on drug metabolism. The research focused on a class of proteins active in the liver known as cytochromes P450. These molecules contain heme, and it was Kappas' long-term interest in metabolic pathways related to heme in the liver that led him to study the effects of controlled, calculated, diets on P450-mediated chemical biotransformations in humans. The results of these studies helped to establish a firm scientific foundation for the developing field of nutritional pharmacology.

Cytochromes P450 are widely studied today because they account in considerable part for individual variations in responses to drugs, hormones, and environmental chemicals by converting them into generally inactive waste products. Knowing that many foreign chemicals increase the activity of P450s, Kappas and coworkers postulated that the major components of foods—which, of course, are complex chemicals in their own right—might also have significant effects on P450 activity and therefore on drug and other chemical metabolism in humans. In a landmark study that was designated as a Citation Classic, they found that normal volunteers who ingested a low-carbohydrate/high-protein diet of fixed, calculated composition cleared their systems of the drugs antipyrine (an analgesic) and theophylline (a bronchodilator) much more quickly than those eating a high-carbohydrate/low-protein diet. This result and subsequent research with other drugs and chemicals including natural hormones highlighted the potential diet-drug-chemical interactions for individuals in normal circumstances and for those on unusual diets; for example, people on certain weight-loss regimens, those who are malnourished or who receive only intravenous glucose for nourishment after surgery, or patients whose diet is altered for treatment of conditions such as obesity, atherosclerosis, and diabetes. The findings of these studies also raised the intriguing possibility of future use of specific food components to regulate the metabolic disposition of selective drugs or even of natural hormones such as estrogens, thus leading to the use of such dietary substances as novel "medications."

Attallah Kappas received an AB degree from Columbia (1947), following completion of his military service; and an MD degree from the University of Chicago (1950). He undertook post-graduate training at the Memorial Sloan-Kettering Cancer Center (MSKCC) and the Peter Bent Brigham Hospital, returning to Chicago in 1957. He was recruited to The Rockefeller University in 1967. In addition to heading the Laboratory of Pharmacology, he served successively during the period 1971-1991 as Program Director; Physician-in-Chief; and Vice President. He was a strong advocate of developing close collaborative relationships with Rockefeller's neighboring institutions and held for various periods joint appointments as the Vincent Astor Chair in Clinical Sciences at MSKCC; professorships in Medicine and Pharmacology at Cornell University Medical College; and Co-Directorship of the Rockefeller-Cornell Medical College MD-PhD program. He was a recipient of Commonwealth Fund and John Simon Guggenheim Memorial Foundation Fellowships; The Burroughs Wellcome Fund Special Award in Clinical Pharmacology; and the ASPET Award for Research in Therapeutics of the American Society of Pharmacology and Experimental Therapeutics. He served as an editor of the Journal of Experimental Medicine during 1971-1981. He was appointed the first Nicholson Exchange Professor from Rockefeller to the Karolinska Institute in 1985 and in 1989 became the first recipient of the newly established NIH Award for Excellence in Clinical Research. He is presently Sherman Fairchild Professor and Physician-in-Chief, Emeritus, at The Rockefeller University.

Upcoming Seminars in Clinical Research Speakers

January 23, 2013	Beryl Koblin, PhD	Head, Laboratory of Infectious Disease Prevention, New York Blood Center
January 30, 2013	Deborah Birx, MD	Director of CGH Division of Global HIV/AIDS (DGHA): Centers for Disease Control and Prevention
February 6, 2013	Nicholas Schiff, MD	Professor of Neurology and Neuroscience, Weill Cornell Medical College
February 13, 2013	Mark Anderson, MD, PhD	Chair, Diabetes Research, University of California, San Francisco
February 20, 2013	Thomas Hostetter, MD	Professor of Medicine, Vice Chair for Research, Case Western Reserve University