



SCIENCE FOR THE BENEFIT OF HUMANITY

Center for Clinical and Translational Science e-NEWSLETTER

Center News

Dr. Christopher Austin, New Director of the National Center for Advancing Translational Sciences (NCATS), Visits Rockefeller

By Barry Collier



Dr. Christopher Austin

Dr. Christopher Austin, the Director of the National Center for Advancing Translational Science (NCATS), and Dr. Elaine Collier, Deputy Director of NCATS, visited the Rockefeller University Center for Clinical and Translational Science (CCTS) on March 22, 2013 to learn more about the programs supported by the University's Clinical and Translational Science Award (CTSA). The day was divided into discussions of a number of different topics.

History of Clinical Research at Rockefeller and CCTS Infrastructure

Drs. Barry Collier and James Krueger, PI and Co-PI of the CTSA, provided Drs. Austin and Collier with an introduction to the history and unique features of the Rockefeller University CCTS and Hospital and the many important translational discoveries made in the Hospital. Donna Brassil gave an overview of the CCTS Navigation program, a multidisciplinary effort designed to assist investigators in developing their human subjects protocols. The program has reduced the time to protocol approval while simultaneously insuring the quality of the protocols. It has been especially valuable for trainees and basic scientists who do

not have extensive experience in human subjects research.

Ed Barbour described the comprehensive, self-guiding, electronic system (iRIS) used for protocol development, protocol review by the Advisory Committee on Clinical and Translational Science (ACCTS) and the Institutional Review Board (IRB), and protocol conduct. The iRIS program underwent extensive customization by Rockefeller CCTS senior staff to incorporate important information in protocol development and conduct and links to source documents.

Educational Programs

Dr. Florian Klein and Dr. Manish Ponda discussed their experiences in the CCTS Clinical Scholars Master's degree program and the Rockefeller Early Phase Physician Scientist (REPPS) program, respectively. Dr. Klein has conducted pioneering studies on the efficacy of broadly neutralizing anti-HIV antibodies in reducing viral replication in a murine model of HIV in Dr. Michel Nussenzweig's laboratory, and those studies have laid the groundwork for future human studies. Dr. Ponda has studied the impact of vitamin D deficiency and repletion on plasma lipids in Dr. Jan Breslow's lab. Dr. Ponda's studies call into question the widespread practice of treating patients with low vitamin D levels with oral vitamin D supplement to improve their lipid profile and offer insights into the mechanism of vitamin D's effects.

Outreach to Basic Investigators and New York Science Collaboration

Nina Papavasiliou, PhD, Tom Tuschl, PhD, and Andreas Keller, MD and Leslie Bellani, PhD from the laboratory of Leslie Vosshall, PhD, discussed their human subjects research projects in the CCTS from the standpoint of basic investigators. Their research spans from studies of immune



Dr. Elaine Collier

cell malignancies, to the role of microRNAs in a variety of diseases, to genetic defects in human odorant receptors and the preference of mosquitos to feed on some humans.

Dr. Robert Darnell discussed Rockefeller University's participation in the New York Genome Center (NYGC) and his role as President of the NYGC. NYGC provides advanced next generation sequencing and bioinformatics to all participating institutes at competitive fees and high quality. This is a vital resource for Rockefeller scientists.

Bringing Science to the Clinical Research Enterprise

Dr. Barbara O'Sullivan described her novel role as a Research Hospitalist providing support to investigators, especially those without a medical background, and insuring patient safety through hospital policies and procedures.

Dr. Rhonda Kost described the centralized research participant recruitment program she has developed to assist investigators in completing their studies rapidly. By centralizing and standardizing the process, investigators can assess the progress of the recruitment process and,

Michelle Lowes, MD, PhD Promoted to Associate Professor of Clinical Investigation

By Michelle Romanick

Dr. Michelle Lowes was recently promoted to Associate Professor of Clinical Investigation in the Laboratory for Investigative Dermatology. Dr. Lowes is a graduate of the Clinical Scholars Program, and is a current member of the Rockefeller University Early Phase Physician-Scientist (REPPS) group. She obtained her medical degree, PhD and dermatology training in Australia. Dr. Lowes has been an NIH-funded investigator since 2006, and has also received funding from The Doris Duke Foundation, The Dana Foundation, the National Psoriasis Foundation, and the Rockefeller University Clinical and Translational Science Awards (CTSA).

Dr. Lowes is studying the chronic inflammatory skin disease psoriasis, mainly from a “dendritic cell-centric” point of view. The lab first described a population

of inflammatory dermal myeloid dendritic cells, which are as abundant as T cells in psoriasis skin lesions. She is the recipient of an NIH independent investigator RO1 grant entitled, “Origin and Function of Inflammatory Dendritic Cells in Psoriasis.” Her research focuses on identifying the precursors of these inflammatory dendritic cells. These precursor cells offer an attractive therapeutic target since inhibiting entry of dendritic cells into the skin could prevent inflammatory skin lesion development, as well as treat existing lesions. Her experiments will enhance our knowledge of monocyte populations and the dendritic cells and macrophages they give rise to, and provide insights into the development of new treatment protocols that target these cells in psoriasis and potentially other autoimmune diseases.



Michelle Lowes MD, PhD

Dr. Edgar Charles, Clinical Scholar Graduate, Joins Merck Research Laboratory

By Michelle Romanick



Edgar Charles, MD, PhD

Dr. Edgar Charles came to Rockefeller in 2004 as a Clinical Scholar in the laboratories of Charles Rice, Ph.D. and Lynn B. Dustin, Ph.D. His studies focused on patients who are infected with hepatitis C virus (HCV) and who subsequently developed autoimmune disease. Dr. Charles received his B.A. from the University of Chicago and his M.D. from the University of Alabama. He completed his residency in Internal Medicine and fellowship in Infectious Diseases at New York University School of Medicine.

Dr. Charles then joined the Rockefeller University Clinical Scholars Program and earned a Master's degree in Clinical and Translational Science. Thereafter, Dr. Charles helped launch the Rockefeller Early Phase Physician Scientist (REPPS) program, designed to help junior investigators achieve scientific independence.

Dr. Charles's research interest was largely driven by his clinical experiences during internal medicine residency and infectious diseases fellowship at NYU/Bellevue. He had the opportunity to care for patients with hepatitis C virus infection, many of whom had serious complications from their disease, with no prospect of effective treatments in sight. He conducted translational research on the immunopathogenesis of HCV infection, with a view to improving the lives of those suffering from chronic viral infections.

Dr. Charles joined the Merck Research Laboratories in the winter of 2012 as Director, Clinical Research, Infectious Diseases, Emerging Markets. In this role, Dr. Charles designs and executes clinical trials of novel therapeutics for the treatment of infectious diseases. Additionally, he authors the clinical sections of regulatory filings, supports document filing activities and interactions with regulatory agencies, and evaluates scientific and business development opportunities in emerging markets with the goal of improving human health through the development of better medicines.

When asked how the Clinical Scholars and REPPS programs prepared him for his current position, Dr. Charles commented, “The Clinical Scholars program and REPPS program provided me with an unparalleled opportunity to train as a physician-scientist.

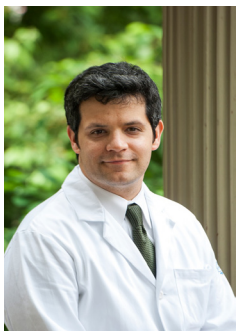
When I joined, the program was one of only several in the country that offered clinicians a significant amount of protected time in the lab. During fellowship, I worked on HIV immunopathogenesis in Fred Valentine's lab at NYU. I knew that I wanted to continue at the bench after fellowship, and when I heard about Rockefeller's Clinical Scholars' Program, I was intrigued. I had been following the work of Charles Rice and Lynn Dustin, and given my clinical interests, it was a great fit for me to join their labs.

In addition to providing me with an intensive laboratory experience and access to the Hospital's extraordinary clinical research facilities, the programs provided an exciting milieu of dedicated translational researchers. Through this group of peers and mentors, I learned how to conduct rigorous translational research. The didactic program formally introduced me to many topics pertaining to commercial drug development; this training has been very relevant to my activities at Merck.”

New Clinical Scholars Join the Center for Clinical and Translational Science

By Michelle Romanick

Five new Clinical Scholars joined the Rockefeller University Clinical Scholars Program on July 1, 2013: Drs. Jose Aleman, Avi Levin, Lotta von Boehmer, Taia Wang, and Ethan Weinberg. Additionally, with support from the Center for Clinical and Translational Science, three medical students joined the Year-Off Training Program for Medical Students in Clinical and Translational Science: Thomas Heineman, Jessica Posada, and Mariya Rozenblit. Below are brief biographies and research interests of the new Scholars and medical students. Please join us in welcoming them.



Jose Alemán, MD, PhD
jaleman@rockefeller.edu
Mentor: Drs. Jan Breslow and Peter Holt

Dr. Jose Alemán received his MD and PhD from Harvard Medical School. During his PhD in Medical Engineering at the Massachusetts Institute of Technology, he developed metabolomic and flux analysis techniques to elucidate insulin-resistant metabolism in transgenic mice in collaboration with investigators at the Joslin Diabetes Center. He completed his Internal Medicine Residency and Endocrinology Fellowship at Weill Cornell Medical Center. During the current year, Dr. Alemán has been studying obesity-associated inflammation and its chronic disease consequences in Type 2 diabetes, cardiovascular disease, and cancer in Dr. Jan Breslow's lab. Dr. Alemán will continue his studies as a Clinical Scholar, including a weight loss intervention study to assess reversal of obesity-associated inflammation, and deployment of noninvasive spectroscopic detection of adipose-tissue inflammation.



Avi Levin, MD
alevin@rockefeller.edu
Mentor: Dr. Hermann Steller

Dr. Avi Levin received his MD from The Hebrew University Hadassah Medical School, Israel, and he completed his Internal Medicine Residency and Gastroenterology Fellowship at Hadassah Medical Center. As a Clinical Scholar in Dr. Steller's lab, Dr. Levin will be studying the role of apoptosis in the development of colon cancer, bowel wall injury healing, and the compensatory response to massive intestinal resection resulting in short bowel syndrome.



Lotta von Boehmer, MD
lvonboehme@rockefeller.edu
Mentors: Dr. Michel Nussenzweig

Dr. Lotta von Boehmer received her MD from the University of Zurich, Switzerland, and completed her Internal Medicine and Medical Oncology Fellowships at the University Hospital in Zurich. As a Clinical Scholar in Dr. Nussenzweig's lab, Dr. von Boehmer will analyze the function and development of B lymphocytes in cancer and HIV positive patients.



Taia Wang, MD, PhD
twang@rockefeller.edu
Mentors: Drs. Jeffrey Ravetch and Sarah Schlesinger

Dr. Taia Wang received her MD and PhD from the Mount Sinai School of Medicine. During her PhD in the Department of Microbiology, she studied innate and adaptive mechanisms of broad-spectrum protection against influenza viruses. As a Clinical Scholar in Dr. Ravetch's lab, Dr. Wang will be studying factors regulating the composition of IgG Fc glycans in humans and the role that Fc glycans may play in the evolution of humoral immune responses.

continued on Page 4

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

continued from page 3



Ethan Weinberg, MD
eweinberg01@rockefeller.edu
Mentor: Dr. Sohail Tavazoie

Dr. Ethan Weinberg received his MD from the University of Maryland School of Medicine and then completed his Internal Medicine residency and Gastroenterology Fellowship at New York Presbyterian Hospital. As a Clinical Scholar in Dr. Tavazoie’s lab, Dr. Weinberg will be characterizing colorectal cancer metastasis using a xenograft mouse model in which tumors surgically resected from patients are engrafted into immunodeficient mice. He will also focus on the development of agents to target microRNAs that affect signal transduction in metastatic colorectal cancer.

Year-Off Training Program for Medical Students



Thomas Heineman
teh2003@med.cornell.edu
Mentor: Dr. Agata Smogorzewska

Mr. Thomas Heineman is currently a third year medical student at Weill Cornell Medical College. His research project will be to study DNA damage responses in human embryonic stem cells (hESc) with abnormalities in the Fanconi anemia pathway, as well as the creation and study of skin equivalents derived from these human embryonic stem cells.



Jessica Posada
JESSICA.POSADA@UCDENVER.EDU
Mentor: Dr. Sohail Tavazoie

Ms. Jessica Posada is currently a fourth year medical student at the University of Colorado, Denver. Ms. Posada’s research project will focus on cancer progression in malignant melanoma, investigating the mechanism by which ApoE mediates its robust suppressive effects on angiogenesis.



Mariya Rozenblit
mariya.rozenblit@mssm.edu
Mentor: Dr. James Krueger

Ms. Mariya Rozenblit is currently a third year medical student at the Mount Sinai School of Medicine. She will study the pathogenesis of atopic dermatitis and the effects of cyclosporin A treatment on barrier defects in patients with atopic dermatitis.

Dr. Christopher Austin, New Director of the National Center for Advancing Translational Sciences (NCATS), Visits Rockefeller

continued from Page 1

if necessary, modify the advertising or the protocol in response to the data obtained.

Lynda Olender, RN, ANP provided information on the mission of the Helibrunn Center for Research Nursing and the programs it has initiated to advance Research Nursing as a specialty practice. Supported by a \$5 million endowment, the Center is creating educational programs and a novel fellowship program.

Building Tools for Investigators Worldwide

Shamim Mollah reviewed the progress of the Center's human phenotyping initiative for bleeding disorders, a collaboration among Ed Barbour, Shamim Mollah, Barry Collier and a past Clinical Scholar, Andreas Mauer. The project includes the development of an ontology of all bleeding symptoms, the creation of a questionnaire with electronic data entry, the standardization of the medical language employed, and the ready availability of the instrument via the internet to all investigators. The Rockefeller CCTS group also participated in the creation of the International Society on Thrombosis and Haemostasis (ISTH) Bleeding Assessment Tool (BAT). Based on the success of the Rockefeller initiative, the ISTH invited Rockefeller to host the ISTH-BAT and Rockefeller has taken on that responsibility. A number of investigators around the world are already using the system, including ones in Italy, Canada, and the U.K. Ed Barbour described a parallel effort to enhance the electronic infrastructure of the International Fanconi Anemia Registry to support advanced genotype-phenotype relationships.

Michelle Romanick provided information on the electronic survey and database developed by the Rockefeller CCTS that is designed to track the career development of graduates from the CCTS training programs (GTSS). The survey was specifically designed so that it could be adopted easily by other CTSA's and 11 other CTSA's have already done so. To facilitate survey completion and data aggregation, each graduate's survey is prepopulated with data from PubMed about publications, Exporter about grants, ClinicalTrials.gov about clinical

studies, and PatentLens about patents.

Dr. Knut Wittkowski provided information about the non-parametric statistical methods he has developed (μ STAT) to facilitate the analysis of clinical and translational studies, and in particular its application to genome-wide association studies (GWAS).

The latter application allows for more refined analysis based on a smaller number of participants.

Dr. Kost also described the Research Participant Perception project she has led, including the development of a validated survey to assess participants' perceptions of their research experience, the fielding of the survey at 15 NIH-supported clinical research centers, and the analysis of more than 4,900 completed surveys. This study is the most extensive sampling of research participants' perceptions and provides vital outcomes data for assessing the effectiveness of informed consent procedures and the conduct of clinical investigation.

Community Engagement and Community Collaborations

Dr. Rhonda Kost and Nancy Jenkes described the CCTS Community Engaged Research program that is co-led by Dr. Jonathan Tobin and Dr. Kost. They provided details on the Community-Acquired Methicillin Resistant Staphylococcal Aureus (CA-MRSA) project, which includes six federally qualified community health centers, Clinical Directors Network (CDN), which is led by Dr. Tobin, and Dr. Alex Tomasz's laboratory at Rockefeller. This bidirectional project combines state of the art clinical care with advanced microbial DNA analysis to track the epidemiology of this serious infection in the community, providing important new information that may allow improved interventions to prevent recurrent disease.

Dr. Peter Forgacs, a Clinical Scholar co-mentored by Drs. Nicholas Schiff of Weill Cornell Medical College and Don Pfaff of Rockefeller, explained his project to assess patients in the minimally conscious state in a specially designed suite of rooms in the Rockefeller University Hospital with

advanced cabling to support EEG and visual monitoring. The study was many years in development. Several patients have already been evaluated and their EEG data are providing new insights, with some patients' EEGs showing evidence of receiving auditory stimuli and responding appropriately to a motor command even without external evidence of a response.

Enabling Therapeutic Development

Dr. Fraser Glickman described the new Rockefeller Therapeutic Discovery and Development Interest Group (TD²IG), which brings together investigators with an interest in therapeutic development, as well as the high throughput screening facility that he leads.

Dr. Mina Pastagia recounted her experience in developing a phage lytic enzyme isolated by Dr. Vincent Fischetti that lyses Staphylococci as a topical therapeutic agent during her training as a Clinical Scholar. Since graduating she has continued her work on developing phage lytic enzyme treatment for other indications.

Dr. Barry Collier concluded the day by describing a new joint initiative by Rockefeller University, Memorial Sloan-Kettering Cancer Center, and Weill Cornell Medical College to develop a tri-institutional therapeutic discovery and development initiative (Tri-I TDI). The program will provide the resources for promising projects to traverse the proverbial "Valley of Death," including medicinal chemistry, toxicology, formulation, and regulatory support. The institutions are also considering partnering with a pharmaceutical company to help provide some of these resources.

At the end of the day, Dr. Austin and Dr. Collier expressed their appreciation for the amount of information they received about CTSA-supported scientific discovery at Rockefeller.

Study of Recovery of Consciousness at Rockefeller University Hospital Involves Collaboration with Weill Cornell Scientists

By Nicholas Schiff and Peter Forgacs

Severe brain injuries may produce coma, a state of unarousable unresponsiveness. While many patients recover from coma quickly, others may remain indefinitely in different states that are collectively known as "disorders of consciousness." These syndromes include the vegetative state, which is a condition distinguished from coma by intermittent eye opening despite total unresponsiveness, the minimally conscious state, which is characterized by intermittent and inconsistent responses to external stimuli, and the confusional state, in which patients develop communication systems but remain limited in their capacity to organize and sustain consistent communication.

There are currently an estimated 250,000 to 300,000 people in the U.S. who are in a minimally conscious state. These patients typically live in long-term care facilities or in their homes with full-time caregivers. Up until the last decade, patients with severe injuries to the central nervous system were uniformly thought to have no chance for meaningful recovery if impaired conscious persisted for more than 6 months or 1 year, depending on the etiology. However, more recently, several landmark observational studies have demonstrated that some patients may recover over prolonged periods of time following their brain injuries. Late recoveries have in some instances been linked to the introduction of medications,

but typically patients have spontaneously regained consciousness. Understanding the underlying biological mechanisms of this recovery process in the severely injured brain and developing novel methods for detection of possible preserved elements of consciousness has been the focus of Dr. Nicholas Schiff, the Jerold B. Katz Professor of Neurology and Neuroscience at Weill Cornell Medical College and his team. Dr. Schiff, Director of the Laboratory of Cognitive Neuromodulation at Weill Cornell is a physician scientist with broad interests in the area of neurological disorders of consciousness. His research bridges basic neuroscience and clinical investigative studies of the pathophysiology of impaired consciousness, the neurophysiological mechanisms of arousal regulation, and the effects of deep brain electrical stimulation techniques on forebrain integration.

Dr. Schiff leads the study of patients recovering from disorders of consciousness at The Rockefeller University Hospital. In preparation for the study, patient rooms in The Rockefeller University Hospital were extensively reconfigured to support the monitoring equipment and a dedicated staff observation room was created. Patients started to be studied in the second half of 2012. The Clinical Scholar working with Dr. Schiff is Dr. Peter Forgacs who completed his Internal 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. Subjects are studied in a dedicated room located in the inpatient floor of the Hospital over 2 – 4 days. During the hospital stay, the subject's spontaneous behavior and brain activity is continuously recorded using video-EEG equipment. Real-time remote observation of the subject is also possible from a separate reviewing room on the same hospital floor. A range of behavioral paradigms are employed to assess the subject's language comprehension, response to non-linguistic stimuli (such as humor or music), and their ability to follow auditory commands or communicate using spoken language, gesture or novel measurement tools that can detect mental imagery.

The study at the Rockefeller University Hospital affords the study an optimal quiet setting for study procedures and includes a multidisciplinary team effort to support the care of these subjects.

Collaborative studies at Rockefeller and Cornell are aimed at improving diagnostic assessments and better understanding of recovery mechanisms of consciousness in people with severe brain injury. The goal is enhance opportunities for people with severe brain injuries to regain their mental functions and thus improve the quality of their lives.

Maija Williams, CCTS Administrative Director, Receives Healthcare Leaders of New York Early Career Healthcare Executive Regent's Award

By Maija Neville-Williams



Administrative Director Maija Williams received The Healthcare Leaders of New York Early Career Healthcare Executive Regent's Award at the Healthcare Leaders of New York Annual Gala and Awards Presentation June on 12, 2013.

This award recognizes individuals who have significantly contributed toward the advancement of healthcare management excellence and the achievement of the goals of the American College of Health Care Executives.

Candidates are evaluated on leadership ability, innovative and creative management, executive capability in developing their own organization and promoting its growth and stature in the community, participation in local, state, hospital and health association activities, participation in civic/community activities and projects, and participation in College activities and interest in assisting the College in achieving its objectives.

Clinical Scholars Program Celebrate New Graduates, Drs. Florian Klein and Giralдина Trevejo

By Michelle Romanick

Dr. Florian Klein and Dr. Giralдина Treveo received Masters' of Clinical and Translational Science degrees in June 2013. A dinner celebrating the Scholars and their mentors was held on June 10, 2013.

Dr. Florian Klein studied the function of B lymphocytes and the development of antibodies in HIV-1-infected patients, in particular antibodies with broad neutralizing activity against HIV-1 in Dr. Michel Nussenzweig's laboratory. He plans to continue his research in Dr. Nussenzweig's laborator as an as Assistant Professor for Clinical Investigation to further investigate Broadly Neutralizing antibodies in HIV-1 therapy.

Dr. Giralдина Trevejo's research in Dr. Jean-Laurent's laboratory focused on finding a new gene associated with increased risk of recurrent pneumococcal infections in early childhood using whole exome sequencing. Once the candidate gene is identified, functional studies will be conducted. Dr. Trevejo will continue her research career as a postdoctoral Fellow in Dr. Jay Koll's laboratory at the University of Pittsburgh Children Hospital studying the pathophysiology and increased control of pneumococcal pneumonia.



Drs. Barry Coller, Sarah Schlesinger, Giralдина Trevejo, Florian Klein, and James Krueger

Clinical Directors Network, CCTS, and Community Health Centers Collaborate to Study Serious Community Acquired Infection

By Jonathan Tobin

Introduction

The Rockefeller University Center for Clinical and Translational Science (CCTS) and Clinical Directors Network (CDN— www.CDNetwork.org), a primary care practice-based research network (PBRN), have collaborated closely since 2009 to build the Community Engaged Research Core (www.Rockefeller.edu/ccts/communityengagement), a component of the NIH-funded Clinical and Translational Science Award (CTSA). Together, they developed and implemented an innovative model that covers the full-spectrum of clinical and translational research from laboratory science (T1, T2) to clinical science (T3) and population health science (T4). They accomplished this by designing and conducting rigorous comparative effectiveness research (CER) and implementation science studies in partnership with CDN's member Federally Qualified Health Centers (FQHCs), with embedded mechanistic studies carried out in the laboratories of The Rockefeller University.

Community-Academic Collaboration

The Community-Acquired MRSA Project (CAMP) provides an example of the robust infrastructure Rockefeller and CDN have developed for conducting practice-based research and learning in collaboration with FQHC clinicians and other community-based partners, designed to understand the genotype and phenotype of CA-MRSA in the NY Metropolitan area, as well as to identify potential risk factors for CA-MRSA transmission and re-infection. Funded initially by a Rockefeller CCTS pilot grant, and subsequently awarded a one year infrastructure grant from the NIH National Center for Advancing Translational Science (NCATS), CAMP has brought together practicing clinicians from six CDN FQHCs in Manhattan, Bronx, Brooklyn, and Westchester with Rockefeller Head of Laboratory Dr. Alexander Tomasz and his colleagues to learn together about best practices in the diagnosis and management of skin and soft tissue infections (SSTIs). A previous study conducted by Drs. Tomasz and Herminia de Lencastre had developed a hospital surveillance network to study healthcare acquired MRSA (HA-MRSA) among NYC and Westchester Hospitals, and the CAMP Health Centers were selected from these same communities.

Study Design

The prospective observational study protocol was carefully planned through a highly engaged participatory design process that included the FQHC clinician-investigators and Health Center support staff, and designed to maintain the standard clinical workflow so as not to disrupt patient care. FQHC clinical staff identify and obtain informed consent from patients, and then the CDN research staff complete the baseline survey (including a description of CA-MRSA symptoms, medical history and related comorbidities, dermatological symptoms, quality of life, health care services utilization, social networks, and potential environmental exposures). A ruled digital photo of the lesions is obtained by the FQHC clinicians before treatment, which generally involves incision and drainage as per guidelines from the Center for Disease Control. One month after the initial visit, a follow-up telephone interview assesses antibiotic adherence, symptoms, and clinical response. Three months after the index infection, a detailed review of the patient's electronic health record (EHR) is conducted to identify any follow-up visits to the FQHCs for SSTIs and related problems, further antibiotic prescriptions, laboratory test results, as well as any subsequent admissions to hospitals or emergency departments. In addition to the detailed clinical, behavioral, and epidemiologic data, biological specimens of the wound, as well as nasal surveillance cultures, are sent to Bio-Reference Laboratories, a local commercial clinical microbiology lab, for bacterial species identification, as well as routine culture and sensitivity testing. Bio-Reference then transports all confirmed Staphylococcal isolates, whether they are resistant or sensitive to methicillin (MRSA and MSSA, respectively) to Dr. Tomasz's Laboratory of Microbiology and Infectious Diseases at Rockefeller for confirmation, identification, and molecular and genetic testing, including multi-locus sequence typing (MLST), spa typing, determination of the unique SCCmec cassettes carrying the resistance determinant *mec A*, and pulse field gel electrophoresis (PFGE). A nested sub-study also examines a wider range of surveillance cultures obtained from multiple sites on the patient's body in order to determine whether there is clonal heterogeneity of MRSA subtypes within patients.

Study Progress and Preliminary Findings

The infrastructure study enrolled 129 patients with SSTIs across the 6 FQHCs. Of patients enrolled, 40% of wound cultures were MRSA+, 16% of nasal cultures were MRSA+, 16% of wound cultures were MSSA+, and 23% of nasal cultures were MSSA+. Those who were carriers of Staphylococci in their nasal cavity had a significantly increased likelihood of having a positive wound culture for MRSA (OR=5.33 95% CI: 1.79-15.88, $p=0.0013$) or MSSA (OR=7.93 95% CI: 2.85-22.08, $p\leq 0.0001$). Those patients with an MRSA+ nasal culture were more likely to report influenza (OR = 7.87, 95% CI: 2.26-27.41) and non-intravenous drug use, such as marijuana or cocaine (OR = 4.05, 95% CI: 1.24-13.29), suggesting a potential nasopharyngeal route of transmission. Both MRSA and MSSA were highly resistant to penicillin, but not to oxacillin (both antibiotics belong to the beta lactam family). USA300 was the predominant PFGE strain type among MRSA+ cultures (85%).

Study Dissemination

Dissemination activities have focused on reaching multiple audiences: practicing clinicians, clinical and translational scientists, and the public. Dissemination to clinicians has involved a combination of grand rounds conducted onsite at CDN Health Centers and online via CME-accredited webcasts (see www.CDNetwork.org/Rockefeller) presented by two alumnae Clinical Scholars, Drs. Mina Pastagia, and Teresa Evinger, as well as by Drs. Alexander Tomasz, Herminia de Lencastre, and Vincent Fischetti. Preliminary study findings were presented at the 2013 meeting of the Association for Clinical and Translational Science (ACTS) conference 2013 in Washington, DC by Dr. Shirish Balachandra, a clinician-investigator from Urban Health Plan, Bronx NY and Dr. Maria Pardos de la Gandara, a post-doctoral fellow in the Tomasz Lab. Another poster was presented at the 13th Conference of the International Society of Travel Medicine in Maastricht, Netherlands (May 2013) by Nancy Jenks, FNP, a family nurse practitioner from Hudson River Health Care (Peekskill NY www.HRHCare.org). Dr. Tobin will present the result of the study at the AHRQ-North American Primary Care Research Group (NAPCRG) Annual Practice-based Research Network (PBRN) Conference in Washington DC (June 2013). MRSA community

[Continued on page 11](#)

Joel Correa da Rosa, Ph.D. Joins the CCTS Biostatistics Group

By Michelle Romanick

Joel Correa da Rosa, Ph.D. joined the Center for Clinical and Translational Science (CCTS) and the Krueger Laboratory as Research Associate in Biostatistics. Dr. Correa da Rosa assists researchers in the design of their experiments, sample size evaluation, selection of appropriate statistical methodology, and performance of statistical data analysis.

Dr. Correa da Rosa received his Bachelor's degree in Statistics at the National School of Statistical Sciences in Rio de Janeiro, Brazil, his Master's degree in Statistics at the University of Campinas in San Paolo, Brazil, and his Ph.D. in Decision Support Methods at Pontifical Catholic University of Rio de Janeiro. He also attended the Stockholm School of Economics as a visiting student during his doctoral work.

Before joining CCTS, Dr. Correa da Rosa was Lecturer at Federal Fluminense University in Rio de Janeiro and a researcher at Active Documentation and Intelligent Design

Laboratory of Institute of Computing at Federal Fluminense University. He taught statistics at the undergraduate and graduate levels for multiple courses, provided statistical support to researchers in the petroleum industry, and assisted researchers in diverse disciplines at the Federal Fluminense University.

Dr. Correa da Rosa commented on why he was excited about joining Rockefeller University, "I really like to perform data analysis and to think about statistical modeling of phenomena in biology and health sciences. The era of Big Data brings any challenges for data analysis and creates a tremendous opportunity for developing methodologies that could help translational science. I am looking forward to assisting researchers in CCTS to strengthen their publications with appropriate statistical data analysis. The application of statistics in these fields fascinates me."



Joel Correa da Rosa, Ph.D

Andrea Leinberger-Jabari, New Community Engagement Specialist

By Michelle Romanick

Andrea Leinberger-Jabari, MPH joined Rockefeller University in March 2013 as the Community Engagement Specialist for the Center for Clinical and Translational Science. In this role as the Community Engagement Specialist, Andrea works with Rockefeller University Center for Clinical and Translation Science (CCTS) faculty and trainees as well as key community partners to match health community needs with CCTS research programs. She also works with CCTS leadership to shape strategic goals for the community engagement programs.

Andrea previously was the Assistant Director of Community-Engaged Research Programs at the University of Minnesota's Clinical and Translational Science Institute, where she oversaw the daily operations of this key function. In this capacity, she worked with academic researchers and community partners across the state to build relationships to develop new community-engaged research projects on topics ranging from person-centered care in

rural long term care facilities and doula care for incarcerated women and their infants, to assessment of nutrition in daycare centers.

Andrea also developed a training program for community partners on the basics of conducting health research with academic partners. Andrea holds a BA in Anthropology from Arizona State University and earned her MPH in Community Health Education from the University of Minnesota in 2004.

She has more than 10 years of experience developing, managing, and evaluating public health programs, and has been recognized as an emerging leader in public health by the Minnesota Public Health Association and the Minnesota Department of Health. Andrea's research interests include using social network analysis methods to measure community engagement, health disparities, and the role of community health workers in medical homes. Andrea lives in Westchester County with her husband, 3 ½ year old son, and their ancient cat.



Andrea Leinberger-Jabari, MPH

Yale/Rockefeller University CTSA Collaborative Research Day

By Michelle Romanick

On May 16, 2013, 16 members of the Rockefeller University Hospital Center for Clinical and Translational Science (CCTS) visited the Yale Center for Clinical Investigation (YCCI), continuing the tradition of annual Collaborative Research Day meetings between Yale and Rockefeller that began in 2008. This year's event, like those in the past, provided a great opportunity for trainees and junior faculty from both institutions to discuss their current research studies, develop collaborations, and discuss topics of mutual interest. Dr. Robert Sherwin, Director of YCCI and Dr. James Kruger, Co-Director of CCTS warmly welcomed the attendees. The first event of the day was a poster session in which 17 posters were presented and discussed. This was followed by a lively lunch-time discussion.

The afternoon was dedicated to presentations from Yale and Rockefeller faculty. Dr. David Hafler, Gilbert H. Glaser Professor and Chairman of the Department of Neurology at Yale School of Medicine, as well as Neurologist-in-Chief of the Yale-New Haven Hospital spoke on the "Pathophysiology of Human Autoimmune Diseases." His laboratory focuses on the understanding of human autoimmune diseases, investigating naturally occurring human diseases that provide insight into the basic processes of T cell regulation. His lab also emphasizes translating these discoveries into therapies for human diseases.

Dr. Judson Brewer, Assistant Professor of Psychiatry and Medical Director of the Yale Therapeutic Neuroscience Clinic then presented "Train your Mind, Change

Your Brain: Insights From Meditation Using Real-time fMRI." He discussed improved methods to analyze mindfulness linking brain activation patterns during specific meditation techniques to physiological and behavioral measures.

Dr. Manish Ponda, Assistant Professor of Clinical Investigation in the Laboratory of Biochemical Genetics and Metabolism and Attending Physician at The Rockefeller University Hospital presented, "Vitamin D Repletion and Cholesterol: The Uncoupling of Epidemiology and Intervention." He presented his data showing that while higher vitamin D levels are strongly correlated with lower cholesterol levels in epidemiologic studies conducted at Rockefeller and supported by population level data obtained in collaboration with QUEST diagnostics showed that correcting vitamin D deficiency with oral vitamin D supplementation does not translate into lower cholesterol levels. These results challenged the current paradigm that vitamin D supplementation mimics the benefit of naturally higher vitamin D levels. He also shared preliminary data from his new, ongoing trial comparing the effect of oral vitamin D supplementation to ultraviolet light therapy. In contrast to oral vitamin D, light therapy has a beneficial effect on cholesterol levels. These new data may explain the paradoxical finding that supplements fail to reproduce the benefits of naturally higher vitamin D levels.

Dr. Florian Klein, Chief Clinical Scholar and Instructor in Clinical Investigation in the Laboratory of Molecular Immunology gave an oral presentation on his studies using

broadly neutralizing antibodies (BNAbs) in HIV-1 Therapy. BNABs are characterized by being able to potentially neutralize a wide range of different HIV-1 strains. In the laboratory of Dr. Nussenzweig, Florian Klein and his colleagues were able to control HIV-1 infection in humanized mice when these animals were treated with a combination of BNABs. This new therapeutic approach was as effective as the combination of classical anti-retroviral drugs. Moreover, based on the long antibody half-life, HIV-1 infection was controlled for an average of 60 days after the last injection of a combination of BNABs.

Dr. Andrew Goodman, Assistant Professor of Microbial Pathogenesis at Yale gave an oral presentation of his abstract on how resident human-associated microbes play critical roles in the response to nutrients, toxins, and pathogens. His research uses genomics and biochemistry to study the processes of selection and competition that shape these communities.

Dr. Michelle Lowes, Associate Professor of Clinical Investigation in the Laboratory of Investigative Dermatology, and an Attending Physician at The Rockefeller University Hospital presented "Myeloid Dendritic Cells in Psoriasis." Her research studies the chronic inflammatory skin disease psoriasis mainly from a "dendritic cell-centric" point of view.

Drs. Krueger and Sherwin closed the event by acknowledging everyone's participation in creating another successful collaborative event. Rockefeller will host the next Research Collaboration Day in 2014.



Clinical Directors Network, CCTS, and Community Health Centers Collaborate to Study Serious Community Acquired Infection

Continued from page 8

health education sessions have been presented in the communities served by CAMP Health Centers. Rhonda Burgess, RN, of Manhattan's Physician Group disseminated CA-MRSA information at "Cutting for a Cure," a community health fair held by Denny Moe's Superstar Barbershop, Harlem, NY. Dr. Onyinye Okpukpara of Open Door Family Health Center, Ossining, NY, and Franco Barsanti, PharmD of Urban Health Plan, Bronx NY presented health information displays at their FQHCs. Dr. Chamanara Khalida, CDN CAMP Project Manager, along with CDN staff, including Amanda Tsang, MPH, and Brianna D'Orazio, have presented MRSA health education sessions and distributed public health educational materials at several health fairs and barbershops in NYC.

Next Steps

A 2013 pilot study funded by the Rockefeller CCTS has expanded the CAMP infrastructure, building upon the AHRQ-funded Center of Excellence (P30) for Practice-based Research and Learning at CDN, "N2: Building a Network of Safety Net PBRNs." The N2-PBRN brings together eight established PBRNs in New York City, Chicago, Boston, Portland, and Oakland, in addition to creating two "incubator" PBRNs in Washington DC and Brooklyn NY. The goal of the CDN N2-PBRN is to strengthen the research and dissemination infrastructure of each collaborating PBRN so as to accelerate the generation of new clinical knowledge. It seeks to build a community of learning for primary care practices in order to improve medical care quality, patient

safety, and clinical effectiveness by rapidly incorporating new clinical knowledge into practice. The CAMP research team is now exploring the geographical heterogeneity of CA-MRSA and building a platform for rapid dissemination of findings by collaborating with other PBRNs. Under the auspices of N2-PBRN the study protocol is being implemented in three additional PBRNs in Texas, Illinois, and New York, including six additional FQHCs. The pilot study involves collaboration with two established PBRNs, South Texas Ambulatory Research Network, STARNet, San Antonio TX with Christopher R. Frei, PharmD, MSc, BCPS and ACCESS Community Health, Chicago IL with Milton Eder, PhD, as well as an "incubator" PBRN at Lutheran Family Health Center Network with Nonkulie Dladla, MD MSc, Brooklyn NY.

A second 2013 CCTS-funded pilot study (Rhonda Burgess, RN, Manhattan's Physician Group, Co-PI) is reaching out to barbers and beauticians in NYC who may see customers with skin and soft tissue infections. These infections pose an occupational health and safety risk to the "esthetic care providers" (and their families), as well as a risk of infection transmission to other customers.

Since barbershops and beauty-parlors in many urban minority communities are often a source of health information for low-income and immigrant populations with limited English proficiency and limited health care access, this represents a novel way to disseminate public health information about MRSA, as well as to

identify research participants who do not have an ongoing source of health care.

A series of focus groups were also conducted with CAMP patients and clinicians as part of a Rockefeller CCTS Pilot Study (PI: Dr. Rhonda Kost). The data indicated that prevention of recurrence was among the patients' greatest concerns. The FQHC clinician investigators reinforced the data obtained from the patient groups since treating recurrent MRSA infections in their patients is a significant clinical challenge. Among CAMP patients enrolled in the study, the staphylococcal infection recurrence rates were 31% and 39% for MRSA+ and MSSA+ patients, respectively. These data have led to a pragmatic clinical trial of household staphylococcal decontamination and family member decolonization to prevent MRSA transmission and recurrence. In 2012, the Rockefeller comparative effectiveness research (CER) study to test interventions to reduce MRSA re-infection by decolonization of household members and decontamination of household surfaces was selected by the NIH CTSA as a "Use Case" for CER and received the highest score among all proposals submitted to the CTSA. The consortium is currently working on a formal proposal to conduct this study.

Beyond MRSA to Hepatitis C

The CDN-Rockefeller CCTS group is also exploring collaborations with the NYS Department of Health to use the established CA-MRSA research and training infrastructure to establish policies and procedures to implement the new age-based universal screening guidelines for Hepatitis C. Dr. Charles Rice, Head of the Laboratory of Virology and Infectious Disease and a world expert in hepatitis C pathogenesis, is collaborating on this initiative.



Community Engaged Research Core

17 Rockefeller Investigators Complete the Center for Clinical and Translational Science Certificate Program

By Michelle Romanick

On May 31, 2013, 17 investigators from across the Rockefeller campus completed the Clinical and Translational Science Certificate Program sponsored by the Center for Clinical and Translational Science (CCTS). Ten of the 17 participants hold PhD degrees.

The program requires that participants successfully complete two courses over the academic year. In the first course, "Introduction to Clinical and Translational Science," the participants learn about each element of a human subjects protocol (e.g., biostatistical considerations, human subjects protection, study design, and conflict of interest) from senior staff and members of the CCTS in a series of tutorials that are coupled with scientific presentations by translational investigators describe their research. With this background, participants create their own hypothetical human subjects protocols, including an informed consent form. After completing their protocols, the participants function as a mock Institutional Review Board (IRB), reviewing each of the protocols and offering suggestions to insure the optimal design and maximizing participant safety.

The protocols that were submitted in fulfillment of the requirement of the course were of exceptionally high caliber and offered insights into the clinical research interests of the talented group of investigators who enrolled in the program.

The second course, "Introduction to Scientific Techniques in Clinical and Translational Science," was led by Drs. Sarah Schlesinger and James Krueger. This course introduced the students to core resources available at Rockefeller University and their application to address critical problems in human biology. The students learn from the Rockefeller University core resource leaders about the resources available and how to apply them to their research. These presentations are supplemented by investigators who have employed the technique to their human subjects research. The final project of the course involved the students returning to the protocols they developed in the first course and enhancing them by adding new techniques to augment their research design and facilitate testing their hypotheses.

Both courses received positive student evaluations, with 100% of the students reporting that they would recommend participation in the Certificate Program.

As one student wrote,

"It was a great introductory class to human subject study. Having the chance to interact with various investigators and staff with a lot of experience in human subject study was very valuable. Also, writing a study protocol and have a mock IRB session seems to be the best way to put together what we learned from the class. I would definitely recommend this course to my colleagues.

The Certificate Program is next scheduled for the academic year beginning in September 2014.



2012-2013 Certificate Course participants

Immunology meets Bioinformatics: Paving the way to Discoveries in Advancing Translational Medicine

By Shamim Mollah

Since their discovery some 30 years ago, skin-derived dendritic cells (DC) have been recognized as potent antigen presenting cells with critical roles in both the initiation of adaptive immune responses and tolerance of self. The development of vaccines and clinical therapeutics to skin cancers has been hindered by a lack of clarity of the function and development of the diverse DC subsets present in the skin and skin draining lymph nodes. Different DC subsets respond to distinct self and foreign antigen challenges, and exhibit different functional specialization.

A research collaboration between Rockefeller University's CTSA bioinformatics core and Dr. Niroshana (Niro) Anandasabapathy is currently underway focusing on understanding dendritic cell lineage of these DC subsets and their function in the setting of productive immunization. This is a phase 1 clinical trial on a hematopoietin that expands dendritic cells, while also investigating the cellular basis for vaccine and the mechanisms in mice by which this drug acts to improve immune responses.

In particular our study builds on the observation that Langerin-CD11b-dermal DCs (CD11b-DC) are Flt3L-dependent and

strongly Flt3L responsive, which may relate them to classical DCs that have been shown to be more useful for vaccine development.

CD11b-DCs are a low-frequency, heterogeneous, previously uncharacterized migratory DC subset. This project is both very fundamental—looking closely at the cellular requirements for immune priming—and highly translational, bringing a drug into the cancer arena that may improve vaccines. It is also challenging—some of the findings go against the current dogma. The bioinformatics analysis has strengthened and reinforced the functional studies.

Utilizing various custom-developed computational methods and bioinformatics tools, namely GeneSpring (GS) and Ingenuity Pathway Analysis (IPA), we have performed gene expression profiling and pathway analysis using development and functional network analysis of individual dendritic cell subsets. Transcriptome analysis suggests a close relationship of CD11b-DCs to other skin DCs, and transcriptional and lineage relationship into other classical DCs.

This work suggests the previously overlooked CD11bDCs subset may be a

distinct and novel target of therapeutics aimed at enhanced cutaneous immunity. Bioinformatics approaches are employed to identify molecular and cellular regions that can be targeted with specific clinical interventions to provide better insights to the molecular and cellular basis of disease.

Dr. Anandasabapathy currently heads an independent group within Department of Dermatology at Brigham and Women's/ Harvard Medical School and is an Associate Physician/Instructor in Dermatology. She is also an Instructor in Clinical Investigation who completed her post-doctoral work at Rockefeller University in the laboratory of Dr. Ralph M. Steinman and is now a member of Dr. James Krueger's laboratory.

Ms. Shamim Mollah is a bioinformaticist at Rockefeller University who currently leads the bioinformatics analytic core operated under the Center for Clinical and Translational Sciences.

Upcoming Seminars in Clinical Research Speakers

September 4, 2013	Christine Eng, MD	Director, DNA Diagnostic Laboratory , Baylor College of Medicine
September 11, 2013	Robert Schwartz, MD, PhD	Laboratory for Multiscale Regenerative Technologies, MIT
September 18, 2013	Juan Lafaille, PhD	Professor of Pathology and Medicine, NYU
September 25, 2013	David Friedman, MD	Assistant Professor of Medicine, Harvard Medical School
October 2, 2013	Michael Camilleri, MD	Professor of Medicine and Physiology, Mayo Clinic

Clinical Scholars Welcome BBQ

By Michelle Romanick



Discovering the Genetic and Evolutionary Basis of Bacterial Antibiotic Resistance

By Elizabeth (Betsy) Hanson



Tomasz, Alexander

In the 1940s and 1950s the first truly effective antibiotics came into use, including penicillin and methicillin. These drugs transformed medicine, but releasing them into the environment in enormous quantities unleashed a backlash from the microbial world. Powerful selective pressure from antibiotics forced bacterial pathogens into a kind of accelerated evolution: mutants with altered antibiotic resistant target proteins emerged and resistance genes became "mobilized" to spread through many pathogenic species. That is how antibiotic-resistant pathogens such as penicillin-resistant pneumococci and methicillin-resistant *S. aureus* (MRSA) have evolved. Less than five decades after the introduction of penicillin, the rapid emergence and spread of multi-resistant pathogens had begun to pose serious problems to the therapy of infectious diseases worldwide; this was the conclusion of national and international experts that convened in a workshop organized by Alexander Tomasz at The Rockefeller University in 1994.

Tomasz has led the field in investigating bacterial evolution as it occurs in the real life, in vivo, environment of pathogenic microbes. In the 1960s he discovered what later became known as the first "quorum

sensing" factor, a kind of bacterial hormone excreted by individual cells that makes an entire population of bacteria receptive for taking up DNA molecules carrying resistance factors. For example, pneumococcus—one of the most dangerous pathogens producing pneumonia—becomes resistant to penicillin by "borrowing" pieces of foreign DNA from other bacteria. Tomasz found that this enables the pneumococcus to remodel its penicillin target proteins, the so-called penicillin binding proteins, so that they can withstand the assault of the antibiotic molecule. Analysis of this phenomenon by Tomasz and colleagues led to the discovery of a novel survival strategy of bacteria, named antibiotic tolerance. They later found that a single foreign genetic determinant, also encoding a low affinity penicillin binding protein, is the basis of the wide-spectrum antibiotic resistance in methicillin-resistant staphylococci (MRSA). These MRSA strains have become the most frequent agents of serious hospital and community acquired infections in our era. Tomasz's group tentatively identified the actual evolutionary source of the genetic determinant conferring methicillin resistance—the so-called *mecA* gene—in another staphylococcus species that inhabits the skin flora of many wild and domestic animals.

Some of the most powerful antimicrobial agents target the mechanism by which bacteria synthesize a cell wall, leading to unique structural changes in these molecules. The characterization of these changes in the bacterial surface has become one of the major contributions of the Tomasz lab to microbial cell biology.

Once human pathogens such as *Staphylococcus aureus* or *Streptococcus pneumoniae* manage to equip themselves with antibiotic resistance genes, they can then produce antibiotic-resistant clones that can be identified by molecular fingerprinting techniques. The Tomasz lab pioneered in launching the first international network

to study the molecular epidemiology of drug resistant staphylococci, pneumococci and enterococci in collaboration with the Laboratory of Molecular Genetics of the Instituto de Tecnologia Química e Biológica (ITQB) in Portugal. This initiative was the first to demonstrate widespread occurrence of multi-resistant pneumococcal and MRSA clones in hospitals in New York City as well as hospitals and Day Care Centers in twenty different countries in Europe, South America, and Asia.

With the arrival of the era of full genome sequencing the collection of thousands of well-characterized bacterial isolates has become a critical resource for tracing the evolution of antibiotic resistant clones of staphylococci during intercontinental spread— as it was reported in a recent collaborative study with the The Wellcome Trust Sanger Institute. Full genome sequencing was also used by the Tomasz lab to identify genetic steps that accompanied the evolution of antibiotic resistance in vivo in a patient undergoing chemotherapy with the antibiotic vancomycin.

Alexander Tomasz, a native of Hungary, received the PhD in Biochemistry from Columbia University (1963). He then joined the laboratory of Rollin Hotchkiss at Rockefeller as a postdoctoral fellow. At Rockefeller, Hotchkiss and René Dubos were pioneers in launching the antibiotic era, and both had worked under Oswald Avery, who identified DNA as the "transforming factor" that could change a harmless bacterium into a pathogenic one. Tomasz became assistant professor in 1964, associate professor in 1967, and professor and head of laboratory in 1973. In 1998 he was named to an endowed chair in infectious diseases honoring the late Greek microbiologist Plutarch Papamarkou. His achievements have been recognized with the first Hoechst-Roussel Award in antimicrobial chemotherapy from the American Society for Microbiology (1982) and the Selman A. Waksman Award in Microbiology (1987).