The Rockefeller University
SCIENCE FOR THE BENEFIT OF HUMANITY

June 2011

Center for Clinical and Translational Science
e-NEWSLETTER

Center News

New Rockefeller Early Phase Physician-Scientists (REPPS) Program Initiated

By Neil Renwick

Drs. Michelle Lowes, Neil Renwick, Teresa Evering, Sandy Vasan, Marina Caskey, Manish Ponda and Edgar Charles

The RU Center for Clinical and Translational Science is firmly committed to educating the next generation of physician-scientists. In recent years, a number of the RU Clinical Scholars Program graduates have successfully obtained highly competitive, peer-reviewed NIH K08 or K23 Mentored Career Development Awards to transition to academic and scientific independence. Despite the significance of these achievements, these junior physician-scientists face a daunting challenge, given the striking and poorly understood low rate of R01 attainment for new investigators at the national level.

To provide maximal support at this critical career juncture, the RU CCTS has initiated the Rockefeller Early Phase Physician-Scientists (REPPS) program, through which participants will obtain encouragement, resources, and institutional commitment required to achieve scientific autonomy.

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The Rockefeller University Receives AAHRPP Accreditation

By Rhonda G. Kost

On March 16th, 2011, the Association for the Accreditation of Human Research Protection Programs (AAHRPP) announced the accreditation of The Rockefeller University human research protection program (HRPP). In accordance with the AAHRPP model, The Rockefeller program integrates three components, each playing a role to integrate leadership and practice for the protection of the rights and safety of research participants. The three levels are the University, the Institutional Review Board, and investigators themselves. The Rockefeller HRPP is led by Dr. Thomas Sakmar, to whom the IRB, the Clinical Research Support Office, the investigators, and others concerned with human research protections report. Dr. Michael Young is the University official ultimately responsible for human research protections at Rockefeller University.

Research on human subjects has been ongoing at the university since 1910, when the Rockefeller Hospital was established.

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Awards & Honors

Michel C. Nussenzweig, MD, PhD was elected to the National Academy of Sciences.

Agata Smogorzewska, MD, PhD received a Doris Duke Charitable Foundation Clinical Scientist Development Award. http://www.ddcf.org/Medical-Research/Program-Strategies/Clinical-Research/Clinical-Scientist-Development-Award/

Announcements

Chief Clinical Scholar Announcement

Dr. Iddo Ben-Dov will be the Chief Clinical Scholar for the academic year 2011 - 2012. Dr. Ben-Dov is a member of the Tuschl Lab and his research focuses on micro, RNA binding proteins and post-transcriptional regulation in kidney disease.

Administrative Supplement Awards

The Rockefeller CTSA was awarded two Administrative Supplements. The first supplement, led by Dr. Agata Smogorzewska and Mr. Ed Barbour, will bring advanced bioinformatics tools to maximize the information scientists can obtain by carefully studying patients with the rare disease, Fanconi anemia. The Bioinformatics team developed a sophisticated electronic version of the International Fanconi Anemia Registry (IFAR) and created an ontology to describe the relationships between the signs and symptoms of the disease and the laboratory and genetic findings in the patients. Data on more than 1,700 patients have been entered into the system. To enhance the value of the system, Shamin Mollah has led the creation of a prototype program to automatically extract terms from the ontology and map them to concepts in a standardized vocabulary. This will allow investigators the ability to new gain insights into the disease and more broadly into diseases that predispose patients to cancer. The second supplement, led by Drs. Rhonda Kost, Jonathan Tobin and Alexander Tomasz in the category of Community Engagement, will focus on building a community health center-based system for the surveillance and treatment of community-acquired Methicillin-resistant Staphylococcus aureas (CA-MRSA). The project is outlined in greater detail in Dr. Tobin's article on page 4.

3rd Annual Yale-Rockefeller Research Collaboration Day Highlights Genetic Research, Mentoring, and Academic Drug Development

By Michelle Romanick

On March 17, 2011, 17 members of the Rockefeller Center for Clinical and Translational Science and 23 members of the Yale Center for Clinical Investigation and Investigation (YCCI) Medicine Program attended the Third Annual Rockefeller University and Yale University Research Collaboration Day. The event was hosted by Yale and held on the West Campus of the university, which is situated on the former site of Bayer Laboratory.

The Rockefeller Center for Clinical and Translational Science participants

The CTSA programs at Rockefeller University and Yale University have partnered to provide a mechanism for Clinical Scholars, faculty, and staff from both institutions to meet and share scientific ideas and identify opportunities for collaborations. The agenda for the day reflected well the goals for networking and research alliances.

Dr. Robert Sherwin, Director of YCCI and Dr. Barry Coller, Director of CCTS warmly welcomed the attendees. Dr. Sherwin indicated that in order for the CTSA programs "to take maximal advantage of the explosion of knowledge in the basic biomedical sciences, we need to attract the best and brightest students and young physicians to careers in clinical and translational research, give them the training and mentoring required to master a daunting array of research approaches and technologies, and the skills to work effectively within complex interdisciplinary teams, often beyond the walls of their own institutions. The annual CTSA scholar retreat between Yale and Rockefeller University was created to support this goal. We're asking our young trainees to look at problems in a new, more collaborative way and therefore I believe it's important for them to make connections with colleagues doing the same. The informal and formal relationships established by such an approach provides our Scholars with an inside look at an institution with a different, yet closely aligned culture and serves to make the Scholar program at each institution better."

Dr. Coller reflected on the rich scientific heritage between Rockefeller University and Yale University; the institutions share a common mission that includes innovation in translational research. Dr. Coller also noted that the event was taking place on what was formerly the Bayer Laboratory, which reflects the major changes occurring in the pharmaceutical industry and the increasing role of academic investigators in drug development.

Dr. Jean-Laurent Casanova, Senior Attending Physician at The Rockefeller University and head of the St. Giles Laboratory of Human Genetics of Infectious Diseases and Dr. Matthew State, Donald J. Cohen Associate Professor in the Child Study Center and Associate Professor of Genetics at Yale University led off the day with exciting scientific presentations. Dr. Casanova's talk, "Life-threatening Infectious Disease of Childhood: Single-gene Inborn Errors of Immunity?" highlighted his laboratory's research, which focuses on trying to understand why some children develop a severe clinical illness during the course of an infection while others exposed to the same microbe do not. Dr. State's presentation on "Recent Advances in the Genetics of Autism Spectrum Disorders," addressed the fundamental properties of genetic variation, described the logic underlying the common variant-common disease and the rare variant-common disease hypotheses, discussed the importance of structural as well as sequence variation, highlighted recent results in the genetics of autism, and described the ways in which these findings offer insights into molecular mechanisms underlying autism. Simultaneously his data challenged the current diagnostic nosology in psychiatry. Both talks were extremely well-received by the audience and generated much discussion.

The afternoon was dedicated to panel discussions with representatives from each CTSA site. The topics were Mentor-Mentee Relationships; Developing Bench-to-Bedside Collaborative Relationship; and Drug Development in Academia. Each of the panels' topics invoked a lively and stimulating discussion with the panel members and the audience. Lunch provided another opportunity for members from each university to network, discuss their research and inquire about their colleague's work.

Drs. Coller and Sherwin closed the event with acknowledgements of everyone's participation in creating a successful collaborative event. Rockefeller will host the next Research Collaboration Day in 2012.

Rockefeller University Hospital Achieves Full Accreditation from The Joint Commission

By Cynthia Seidman

On Feb. 26 2011, The Joint Commission (TJC) arrived at the Rockefeller University Hospital for an unannounced three day survey. TJC is a nonprofit organization that inspects hospitals every three years to ensure they meet the highest standards of patient care and safety. This is the second unannounced survey RUH has undergone in the past three years, but unlike past surveys that lasted 2 – 2 ½ days, this inspection lasted 3 full days. Two inspectors were assigned to conduct the accreditation evaluation; a nurse, who meticulously examined medical records, interviewed the nursing staff, and thoroughly reviewed hospital policies, and a Life Safety Specialist, an expert in fire safety issues, who inspected the physical plant and all of the equipment in the hospital building. Based on the extensive review, Rockefeller University Hospital was awarded accreditation for another three years. This successful outcome is due to the superb efforts of the hospital staff coordinated by Ms. Cynthia Seidman, Director of Regulatory Affairs.

New Rockefeller Early Phase Physician-Scientists (REPPS) Program Initiated

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The REPPS program currently has 6 participants*, including Drs. Marina Caskey (NIAID K23 award: HIV-1 vaccine strategies), Edgar Charles (NIAID K08 award: HCV-related autoimmunity), Teresa Evering (NIMH K08 award: Cognitive decline in HIV-1 infection), Michelle Lowes (NIAMS K23 award: inflammatory dendritic cells), Manish Ponda (NIDDK K08 award: atherosclerosis in renal disease), and Neil Renwick (NINDS K08 award: TDP43-related neurodegeneration); for further details please see repps.rockefeller.edu.

The REPPS group has a significant advantage due to mentorship from distinguished scientists at the RU CCTS; currently Profs. Jan Breslow, Lynn Dustin, Jim Krueger, David Ho, Marty Markowitz, Ralph Steinman, and Tom Tuschl are generously committing time and laboratory resources to these junior physician-scientists.

In addition to their scientific activities, REPPS participants are clinically active, with combined expertise in dermatology, infectious diseases, internal medicine, nephrology, and pathology. Each participant is highly dedicated with an exceptional training record, has advanced medical knowledge in their field, has worked nationally and internationally, and is highly adept at articulating medical needs and advocating for their patient populations. The personal (program members come from Australia, Brazil, New Zealand, and the United States) and scientific diversity of the REPPS group fosters a collegial, respectful, and enthusiastic atmosphere for group activities.

The REPPS group will meet monthly to discuss relevant topics in academic medicine and develop expertise while attaining independence. Topics will include: emerging techniques for translational medicine and assay design, grant writing skills, laboratory leadership, mentoring, protection of human subjects, regulatory issues, research ethics, teaching and course design, technology transfer and therapeutic strategies. The group has been charged with identifying experts on and off campus to participate in these discussions and is grateful to the CCTS leadership, particularly Drs. Barry Coller, Jim Krueger, and Sarah Schlesinger, for committing their time and expertise to these discussions. The RU Hospital has an exceptional century-long track record in producing creative and innovative physician-scientists and the REPPS program continues this proud tradition.

*Dr. Sandy Vasan, first chairperson of the REPPS program, has recently accepted a position as project manager overseeing HIV-1 vaccine trials for USAMRIID in Bangkok, Thailand. Dr. Neil Renwick was selected as her successor.

The Rockefeller University Receives AAHRPP Accreditation

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The university later formed an institutional review board (IRB), in accordance with the National Research Act of 1974, charged with ensuring the safety of the hospital's patients.

The IRB formalized informal procedures already in place to assure the protection of human subjects and has revised its procedures continually in response to the evolution of best practices in protecting human subjects. Among its responsibilities, the IRB ensures researchers have been educated in the regulations dealing with human subjects, research protocols are designed to incorporate the highest ethical and scientific principles, and research teams conduct their work accordingly.

Founded in 2001, AAHRPP (http://www.aahrpp.org/www.aspx) is a private, not for profit organization that undertakes the systematic review of human research protection programs with a view toward sound organizational structure, accountability throughout the governance of human protections, three-armed involvement of institution, IRB and investigators, and incorporation of best practices. There are currently 229 organizations accredited by AAHRPP of which 34 are institutions with Clinical and Translational Science Awards. The AAHRPP seal has become a gold standard for human research protection programs, signifying high standards, quality, organization and efficiency.

The Rockefeller University began the accreditation process in early 2010, led primarily by IRB chair Dr. Emil Gotschlich, and assisted by expert consultants. At Rockefeller, in addition to the IRB, the multiple departments provide services that are integrated to support the protection of human subjects, including the Clinical Research Support Office, the Office of Research Facilitation, Research Nursing, Bioinformatics, and Clinical Facilities and Research Resources. Rockefeller completed a 6 month long, two stage process of preparation, culminating in a 3 day site visit in January 2011, a review by the AAHRPP council, and the final conferring of accreditation in March 2011. The first renewal period for AAHRPP accreditation will occur after three years. Subsequent renewals renew on a 5 year cycle.

In the near future, as part of its assessment, the IRB will elicit feedback on its performance in the form of a survey to investigators

Rockefeller Scientists Team Up with Community Health Center Network to Track and Treat Community Acquired Methicillin Resistant Staphylococcus Aureus (MRSA) Infections

By Jonanthan N. Tobin

In order to foster the bi-directional engagement of community-based primary care clinicians with academic researchers, the Rockefeller Center for Clinical and Translational Science (CCTS), Clinical Directors Network (CDN), and six metropolitan NYC-area Community Health Centers (CHCs) are collaborating on a CCTS-funded pilot project on Community Acquired-Methicillin-Resistant Staphylococcus Aureus (CA-MRSA). Clinical Directors Network (CDN – see www.CDNetwork.org) is a primary care Practice-Based Research Network (PBRN) that works with CHCs funded by the Health Resources and Services Administration (HRSA – see www.hrsa.gov) and other healthcare safety-net providers to conduct research and training activities in collaboration with academic health centers. HRSA-funded CHCs provided comprehensive primary care and preventive services to over 16 million low-income, minority and other medically underserved patients in 2010 at over 8000 delivery sites across the USA.

According to the CDC's estimates in 2005, the number of MRSA infections has doubled nationwide, and may be responsible for more deaths each year than HIV/AIDS. CA-MRSA infections, as opposed to healthcare acquired MRSA (HA-MRSA), are defined as bacteriologic confirmed cases where the infection onset is in the community and the patient has no prior health care facility exposure. The true incidence and causes of CA-MRSA are unknown and there is no existing nationwide surveillance system for CA-MRSA. Networks of primary care practices such as Community Health Centers, may represent an existing infrastructure that could be strengthened to create a sentinel network for observing and intervening in CA-MRSA infections.

The CCTS-funded CA-MRSA Project (CAMP) arose out of conversations begun in the Action Committee for Community-Engaged Research (ACCER), co-chaired by Drs. Rhonda Kost and Peter Holt, and builds upon and extends the work of Drs. Alexander Tomasz and Herminia de Lencastre, whose research has included characterizing the molecular epidemiology and evolution of MRSA infections and building a surveillance network of NYC-area hospitals.

Dr. Tomasz is joined by Dr. Jonathan N. Tobin, President/CEO of CDN, who was appointed in January 2011 as Co-Director for Community Engaged Research at the CCTS, and he serves as the Principal Investigator for the pilot project. The CA-MRSA Project (CAMP) was initiated in May 2010 and consists of two phases. During phase I, CDN has identified, engaged, and recruited six CHCs located in Manhattan, Bronx, Brooklyn, and Westchester, adjacent to the hospitals in Dr. Tomasz's hospital network. CAMP will create the infrastructure to assess the of CA-MRSA prevalence and the best practices associated with identifying, diagnosing, preventing and managing CA-MRSA in the CHC primary care settings.

The project activities include providing ongoing interactive continuing medical education (CME) sessions both onsite and online for CHC clinicians that builds on the current Rockefeller-CDN CME program. Most of these educational programs will be provided online via webcast and then stored for future reference (see www.CDNetwork.org/Rockefeller). Other activities involve a bioinformatics component to evaluate the feasibility of harvesting information from CHC electronic information systems, including electronic health records (EHRs), electronic prescribing records (ePrescribing) and clinical laboratory test ordering and test results reporting. This information may be useful for enhancing the phenotyping of CA-MRSA.

Finally, for phase II, the pilot project will explore the use of social network analysis to understand potential risk factors for CA-MRSA transmission and infection, and will establish the feasibility of obtaining biological specimens from community-based sites and transporting them to Dr. Tomasz's lab, where molecular characterization can be carried out beyond the routine culture and sensitivity testing that is provided as part of primary care. Aerobic bacterial cultures will be sent to the CHC's local clinical microbiology lab for species identification (routine isolation and identification procedures) and where appropriate, antibiotic susceptibility testing will be performed using either the minimum inhibitory concentration or the disk agar diffusion method. Staphylococcal isolates from the clinical

Jonathan N. Tobin, PhD, FACE, FAHA

microbiology lab will undergo further confirmatory testing, including antibiotic sensitivity and molecular typing in Dr. Tomasz's laboratory at Rockefeller.

In order to confirm the isolates as CA-MRSA and to identify the particular CA-MRSA clone responsible for the antibiotic resistance, the Tomasz lab will employ the following typing techniques: multi locus sequence typing (MLST), determination of the nature of the surface determinant spa (spa typing), determination of the unique SCCmec cassettes carrying the resistance determinant mec A, and pulse field gel electrophoresis (PFGE).

Educational and community engagement activities carried out to date have included an initial Advisory Committee Meeting held at Rockefeller on December 16th, 2010, where the medical directors and primary care clinicians from each of the six CHCs came together to meet with faculty, scientists and Clinical Scholars from Rockefeller. CHC Participants included Samual Deleon, MD, Claude Parola, MD, and Sara Palamino, NP from Urban Health Plan (Bronx NY), Daren Wu, MD and Onyinye Okpukpara, MD from Open Door Family Health Center (Ossining NY), Christine Kerr, MD and Chinea Carmen, MD from Hudson River HealthCare (Peekskill NY), Sharon Smith MD, Judith Buck NP and Jotir Ramnarine MD from Manhattan Physicians Group (NYC) and Fouzia Syed, MD from Brookdale Family Care Center (Brooklyn NY). Dr. Barry Coller, CCTS Director, welcomed the participants and gave an introduction to the CCTS. Dr. Coller's introductory remarks were followed by presentations on CA-MRSA by Drs. Alexander Tomasz, Herminia de Lencastre, and Mina Pastagia. The CHC

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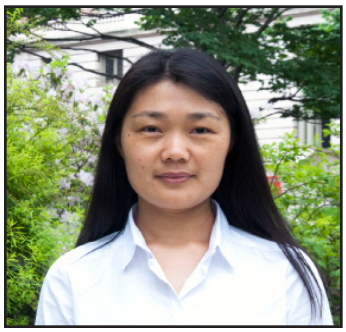
Meet the Scholar: Shen-Ying Zhang, MD, PhD

By Michelle Romanick



Shen-Ying Zhang, MD, PhD

Dr. Shen-Ying Zhang joined the Clinical Scholars Program at Rockefeller University in 2008. She received her MD from Shanghai Fudan University in China in 1994 and her PhD from Paris Descartes University in Human Genetics and Immunology in 2007. The clinical training in the field of Infectious Diseases she obtained in China awakened her interest in medical research of infectious diseases. Her interest in genetic predisposition to infectious diseases was triggered by Dr. Jean-Laurent Casanova's visit to Shanghai in 2002. Dr. Casanova subsequently invited her to join his Laboratory of Human Genetics of Infectious Diseases (HGID) as a post-doctoral fellow at the Necker Medical School, Paris Descartes University, where she studied the genetic susceptibility to herpes simplex encephalitis (HSE) in children under the joint supervision of Dr. Casanova and Dr. Laurent Abel.

Dr. Zhang and her colleagues were the first to identify autosomal recessive UNC-93B deficiency associated with childhood HSE and they later went on to discover a second genetic abnormality associate with the disease, namely autosomal dominant Toll-like Receptor 3 (TLR3) deficiency. Her work has had major medical implications since affected children can now be offered a molecular diagnosis, families can receive genetic counseling, and more importantly, a treatment based on giving recombinant IFN-α to overcome the defects in the pathway leading to its production in these patients is now available. This research also has additional fundamental implications, as it is the first demonstration that a TLR can play a non-redundant role in host defense in a naturally occurring infection.

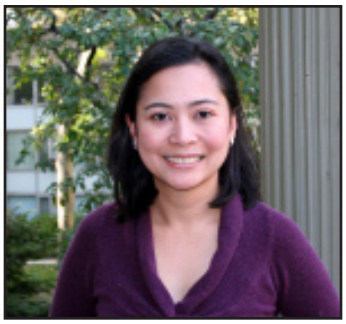
Upon completing her PhD, Dr. Zhang was invited join Dr. Casanova's lab in Paris as a postdoctoral fellow, and later she accompanied Dr. Casanova to the Rockefeller University as a Clinical Scholar and Instructor in Clinical Investigation. Dr. Zhang's current primary research focus is to exploring the molecular and cellular mechanisms of the pathogenesis of HSE by studying the TLR3-interferon circuit and anti-HSV-1 immunity in central nervous system (CNS)-specific cells. In 2009, Dr. Zhang was awarded a CCTS pilot project for a study titled "Cellular dissection of herpes simplex encephalitis in human neural cells." Under the mentorship of Dr. Casanova and in collaboration with Dr. Luigi D. Notarangelo at Harvard Medical School and Dr. Lorenz Studer at Memorial Sloan-Kettering Cancer Center, she is investigating the molecular and cellular mechanisms of the pathogenesis of HSE by using CNS cells that have been differentiated from induced pluripotent stem cells (iPSCs) derived from dermal fibroblasts of HSE patients with known genetic etiologies. She has already achieved a model to investigate the molecular and cellular dissection of the pathogenesis of HSE by using human patient's in vitro differentiated CNS cells from the dermal fibroblasts-derived iPSCs.

During her two years in Dr. Casanova's laboratory at Rockefeller University, Dr. Zhang has also begun to co-supervise younger trainees. This has led to the identification of an autosomal recessive form of TLR3 deficiency and two novel genetic etiologies of HSE due to deficiencies in TNF receptor-associated factor 3 (TRAF3) and TANK-binding kinase 1 (TBK1). These findings further support the hypothesis that HSE can result from inborn errors of the TLR3-interferon pathway. Dr. Zhang has decided to continue her research efforts on the genetic and molecular dissection of viral diseases.

Dr. Zhang has enjoyed the great opportunity offered by the Clinical Scholar program at Rockefeller, and she hopes more clinician scientists could benefit from the Clinical Scholar program, which provides excellent guidance to the clinician scientists on how to transient to an independent medical research career.

Where Are They Now? Kristine Nograles, MD, Clinical Scholars Graduate 2010

By Michelle Romanick



Kristine Nograles, MD

Dr. Kristine Nograles, a 2010 graduate of Rockefeller University Center for Clinical and Transitional Science Master's degree in Clinical and Translational Science Program joined the Merck Research Laboratories in fall 2010 as Associate Director of Clinical Research in Immunology. As part of the Late Stage Clinical Development, her responsibilities include designing and implementing Phase II to Phase III clinical trials to support worldwide drug development. Dr. Nograles's principal goal is to discover and develop safe and effective novel medicines that may save and improve lives around the world.

When asked how the Clinical Scholars Program prepared her for her current position, Dr. Nograles stated, "The hands-on experience of conducting a translational or clinical research project under the supervision of a scientific leader is an invaluable learning experience for anyone seeking a career in patient-oriented research. I had the privilege of working with Dr. Jim Krueger, who is a trailblazer in translational Dermatology research. With his supervision, I was able to conduct research projects that addressed important questions on the pathogenesis of common skin diseases, particularly psoriasis and atopic dermatitis. It is the clear understanding of disease pathogenesis that is key to identifying potential drug targets. In addition to this positive experience, the Clinical Scholars Program provided me with essential tools for the proper conduct of patient-oriented clinical research, including clinical trial design, biostatistics, and the protection of human subjects. I highly recommend the Program!"

Dr. Kruger started, "Kristine was a model student of what it means to do translational research. She was outstanding in taking basic science discoveries generated during research in the laboratory, and applying them to the development of trials and studies in humans. It was a privilege to mentor such an outstanding clinician scientist who will utilize this knowledge in the next steps of her career."

2011 Clinical Scholar's Master Degree Program Graduates

By Michelle Romanick

- Dr. Batya Davidovici accepted a faculty position as a Senior Dermatologist in the Department of Dermatology at the Rabin Medical Center in Israel.
- Dr. Patricia Maningat will continue on in Dr. Jan Breslow's laboratory to complete her studies of statin-induced myopathy.
- Dr. Andreas Mauer is returning to medical training as a cardiology fellow at Massachusetts General Hospital.
- Dr. Jan Davidson-Moncada is returning to medical training as an oncology fellow at the National Cancer Institute in Bethesda.
- Dr. Mina Pastagia will be continuing her studies to develop a lysin antibiotic for clinical use in MRSA infection in Dr. Fischetti's laboratory.
- Dr. Shen-Ying Zhang will continue in the laboratory of Jean-Laurent Casanova at Rockefeller studying the Mendelian genetic basis of rare infectious diseases.

Bionutritionists at Rockefeller University Develop Training Programs For Dietetic Interns and Students

By Andrea Ronning

As part of the Rockefeller University Center for Clinical and Translational Science educational programs, Dianne Meehan, RD and Andrea Ronning, RD have created a core training program for the New York-Presbyterian Hospital dietetic interns and New York University graduate and undergraduate dietetic students who rotate through the Rockefeller Metabolic kitchen in the Department of Nutrition each year.

In their quest to support education in bionutrition nationwide, under the auspices of the Education Subcommittee of the National Association of Bionutrionists (NAB), they polled Bionutrionists at CTSAs across the country about their training programs and preceptors tools. From this experience, they organized projects, selected research articles and developed hands-on-training that resulted in a template that can be modified by each Department of Bionutrition. The template allows the preceptor to select the learning objectives specific to their organization and their dietetic interns.

Two highly valuable, user friendly tools developed in the program that benefits the intern is the calendar function, which establishes a working schedule for the user and a competency checklist that ensures regulatory compliance. The Board of Directors of NAB reviewed the template and approved it. As a result, the Dietetic Intern/Dietetic Student "Preceptor Tool Kit" is now available to all CTSA Bionutrition Departments via

The Bionutrition Department

Meet CCTS Year-Off Medical Student Training Program Graduate: Dr. Austin Pantel

By Austin Pantel

Austin Pantel

After completing my third year of medical school at New York University School of Medicine, I had the privilege of spending a year as a visiting medical scholar in the Center for Clinical and Translational Science Year-off Training Program for Graduate and Medical Students. As a medical student taking care of patients in the hospital, I witnessed the profound effect that new advances in medicine can have on patient care. As a Medical Student Scholar at Rockefeller University, I had the opportunity to engage in research in Dr. Ralph Steinman's Laboratory of Cellular Physiology and Immunology.

With tremendous support from Dr. Steinman and many other generous lab members, I investigated the response of dendritic cells to vaccine adjuvants. I began to understand the process by which new discoveries are made and I enjoyed working through complex problems alongside other laboratory members and collaborators. I quickly realized how much I enjoyed such challenges and knew I wanted to engage in research in my future career.

My laboratory experience was complemented by a formal curriculum in clinical and translational investigation. I enjoyed the weekly tutorials in Clinical and Translational Science where KL2 Clinical Scholars presented selected topics and often discussed their own research. I particularly appreciated interacting with the KL2 Clinical Scholars who have chosen a career as a physician-scientist. As the year progressed, I found myself aspiring to a similar career, though still unsure of my medical specialty.

After I completed my year as a Medical Student Scholar, I returned to medical school searching for a specialty that would enable me to combine patient care and research. I quickly discovered the field of diagnostic radiology and was drawn to residency programs that integrated research into the clinical residency. With great support from Rockefeller, I was able to match into my first choice, the research track of the radiology training program at the Hospital of the University of Pennsylvania. This five-year track includes at least one year of devoted research time.

My year at Rockefeller enriched my time in medical school and helped me realize that research is important to my ultimate career satisfaction. I am truly grateful to have had the opportunity to have worked at such a special place.

Team Rockefeller Walks to Cure Psoriasis

By Caroline Melendez and Rhonda G. Kost

On May 1st, Recruitment Staff and members of the research community from The Rockefeller University, and the Center for Clinical and Translational Science (CCTS) joined hundreds of others at the New York Botanical Gardens to raise awareness for the fight to treat and cure Psoriasis.

For the third consecutive year, Team Rockefeller walked in the Gardens while staff from the Clinical Research Support Office and the Clinical Research Recruitment Outreach and Support Service (CRROSS) spoke to patients and family members about opportunities for participation in translational research.

The Rockefeller University CCTS is a proud sponsor of the Walk to Cure Psoriasis, which serves as a major fundraising effort for the National Psoriasis Foundation. Psoriasis is the most prevalent autoimmune disorder in the United States, affecting as many as 7.5 million Americans. Worldwide up to 125 million people are affected by psoriasis (www.psoriasis.org). The purpose of the Walk is to increase awareness while raising money for education, advocacy, and research.

Researchers at the CCTS conducting research into psoriasis and other skin disorders include Dr. James Krueger, Dr. Michelle Lowes, and Dr. Batya Davidovici.

Caroline Melendez, Stephanie Tigor and Diane Meehan

Rockefeller Scientists Team Up with Community Health Center Network to Track and Treat Community Acquired Methicillin Resistant Staphylococcus Aureus (MRSA) Infections

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clinicians shared their experiences in identifying, diagnosing and managing CA-MRSA in their CHCs, and the challenges associated with providing care for uninsured patients who lack access to laboratory services for diagnosis, surgical consult for treatment, and pharmacies for antibiotic prescriptions.

Following the December kick-off meeting at Rockefeller, three of the CHCs have hosted onsite CME sessions arranged by CDN's Project Manager, Chamanara Khalida, MD, MPH and CCTS Community Engagement Specialist, Bernice Rumala, MA. These CMEs have been presented by Drs. Mina Pastagia and Teresa Evering. Three CME sessions have been held to date at Open Door Family Health Center (Ossining NY), Hudson River Health Care (Peekskill NY), and Urban Health Plan (Bronx NY), with a total of 57 clinicians participating (53% physicians, 30% nurses)

The CHC clinicians, Tomasz Lab members and CCTS staff all actively participated in the discussions. CHC clinicians learned that incision and drainage of the skin infection site is an effective treatment, and the importance of community hygiene in preventing relapses of CA-MRSA infections. RU scientists learned about the difficulties of tracking infected patients, and the treatments commonly used for CA-MRSA in the CHC setting. The extensive information exchange during the CME session strongly demonstrated the value of bridging the scientific advances and improvements in healthcare delivery.

RU and CDN have applied for a supplement grant from the NIH Clinical and Translational Science Award (CTSA – www.ctsaweb.org) Program for expanding the CA-MRSA Pilot Project to further facilitate community engagement and interaction among research institutions and community partners, including CHCs.

In phase II of the CA-MRSA project, CDN will assess the prevalence and risk factors of CA-MRSA by collecting and analyzing samples from patients and performing detailed chart reviews. Ultimately, the data from the pilot study will provide a range of prevalence estimates associated with the diagnosis, treatments and outcomes for CA-MRSA, and will help to build the infrastructure to conduct comparative effectiveness research (CER) studies comparing different approaches to diagnosis, treatment and prevention of CA-MRSA, while understanding the molecular mechanisms of antibiotic resistance in community-based settings. The ultimate goals of the program are to insure that affect patients receive optimal medical care and to develop effective strategies to prevent the spread of the infection based on the epidemiologic data.

Jonathan N. Tobin, PhD, FACE, FAHA is the President/CEO of Clinical Directors Network (CDN) and Co-Director for Community Engaged Research in The Rockefeller University Center for Clinical and Translational Science (CCTS), and is also a Professor in the Department of Epidemiology and Population Health at the Albert Einstein College of Medicine of Yeshiva University.

Clinical Directors Network
The Rockefeller University Center for Clinical and Translational Science
CA-MRSA Pilot Project – Participating Community Health Centers (CHCs)

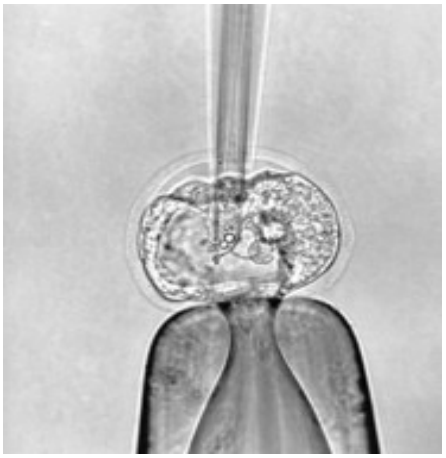
CHC Name	Location	Clinician Name/Degree
Brookdale Family Care Center	Brooklyn NY	Fouzia Syed, MD
Urban Health Plan	Bronx NY	Samual Deleon, MD Claude Parola, MD Sara Palamino, NP
Manhattan E95ST Physician Group	Manhattan NY	Sharon Smith, MD Judith Buck, NP
Manhattan W152ST Physician Group	Manhattan NY	Jotir Ramnarine, MD
Open Door Family Health Center	Ossining NY	Daren Wu, MD Onyinye Okpukpara, MD
Hudson River Health Care	Peekskill NY	Christine Kerr, MD Chinea Carmen, MD

Discoveries Advancing Medicine Vignette
Creating the "Heart-Attack Mouse": A Model for Atherosclerosis

By Elizabeth (Betsy) Hanson

About one-third of all deaths in the United States each year are due to heart disease, most of it caused by atherosclerosis. In this disease process, there is build-up of cholesterol and other materials that alter the inner linings of arteries supplying blood to the heart, leading to blood clots and death of heart muscle tissue (heart attack). Research on atherosclerosis was long hampered by the lack of a small animal model in which to study how plaques of cholesterol form; to unravel the genetic basis for susceptibility to atherosclerosis; and to test new therapies. Mice—among the most convenient laboratory animals—are in fact highly resistant to developing atherosclerosis. But in the early 1990s, Dr. Jan L. Breslow (1943 -) used new genetic techniques to engineer mice lacking a gene called apo E. The mice developed plaques similar to those in humans—and the lesions were exacerbated when the mice ate a high-cholesterol, high-fat Western-type diet. This "heart-attack mouse" transformed scientific research on atherosclerosis.

Dr. Breslow had already pioneered the discovery of human genes that play a role in atherosclerosis. These genes code for molecules called apolipoproteins, which carry cholesterol through the blood. He also was the first to demonstrate that a mutation in one of these genes could lead to atherosclerosis at a young age in humans. Breslow investigated what would happen by removing the gene for apolipoprotein E (apo E) in mice because he knew that apoE on lipoproteins was a signal for their removal from plasma and that human variations in this gene could alter blood levels of low density lipoprotein (LDL)—the "bad" cholesterol that contributes to plaques in arteries.



Scientists inject DNA into mouse embryos. Jan Breslow has developed several such mouse models for reseach on heart disease

Today more than 95 percent of experimental pathology research in atherosclerosis is carried out using the apo E knockout mouse. Not only has it provided a system for studying how lesions form in arteries, it also has given scientists a way to test the effects of other genes on how atherosclerosis develops, by breeding so-called candidate genes onto the apo E knockout mouse background. In addition, when Breslow crossed the apo E knockout trait onto different inbred mouse strains, he found a wide range in the size of the lesions that formed. This indicated modifier genes, and through genetic crosses he has found additional genes involved in atherosclerosis susceptibility. The apo E knockout mouse is also widely used in the pharmaceutical industry to test compounds for treating atherosclerosis.

Dr. Breslow received the AB from Columbia College (1963), the MA from Columbia University (1964), and the MD from Harvard Medical School (1968). After an internship and residency in pediatrics at Boston Children's Hospital and a post as staff associate at the Molecular Disease Branch of the National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda. In 1973 he returned to Boston Children's Hospital as chief of the metabolism division and assistant and then associate professor of pediatrics at Harvard Medical School. He joined Rockefeller University as professor in 1984 and was named Frederick Henry Leonhardt Professor in 1986. He is a senior physician at The Rockefeller University Hospital, where he also served as physician-in-chief in the early 1990s. Among many honors, Breslow has received the American Academy of Pediatrics E. Mead Johnson Award (1984), Germany's Heinrich Wieland Prize in Lipid Research (1991), the American Heart Association's Basic Research Prize (1994), the Bristol-Myers Squibb Award for Distinguished Achievement in Cardiovascular Research (2000), the New York City Mayor's Award for Excellence in Science and Technology (2005), and the American Heart Association's Distinguished Scientist Award (2006). He is a past president of the American Heart Association and has been elected to the U.S. National Academy of Sciences (1995), the Institute of Medicine (1997), and the German National Academy of Sciences (1996).

Dr. Breslow (right) with his student Andrew Plump who made the apo E knockout mouse as part of his thesis work