THE ROCKEFELLER UNIVERSITY HOSPITAL
CENTER FOR CLINICAL AND TRANSLATIONAL SCIENCE

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Center for Clinical and Translational Science

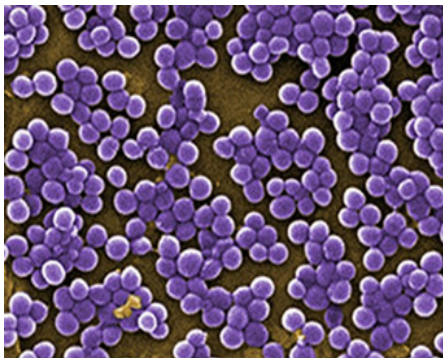
Center News

Rockefeller University and Clinical Directors Network Share $2.8 million Award to Better Prevent Drug-Resistant Infections in the Community

By Jennifer Einstein

A collaborative research team at The Rockefeller University Center for Clinical and Translational Science (CCTS) and Clinical Directors Network (CDN) has received a $2.8 million award from the Patient-Centered Outcomes Research Institute (PCORI) to study a home-based intervention to prevent recurrence of a community-acquired drug-resistant Staphylococcal aurea infection (MRSA). PCORI was established under the Patient Protection and Affordable Care Act to fund research on clinical effectiveness.

The Community Acquired MRSA Project will enroll patients with skin infections, provide English- and Spanish-language health education materials about community-acquired drug-resistant staph infections, and test in a randomized fashion whether household decontamination helps prevent reinfection and transmission.



MRSA up close

An electron micrograph shows clumps of methicillin-resistant Staphylococcus aureus (MRSA) bacteria, the pathogen responsible for an increasingly common community-acquired infection. (Image by Janice Carr, Centers for Disease Control and Prevention.)

The project, known as CAMP2, will be led by Jonathan N. Tobin, president and CEO (CDN) and co-director of community-engaged research and an adjunct faculty member at Rockefeller, Alexander Tomasz, Dr. Plutarch Papamarkou Professor and head of the Laboratory of Microbiology and Infectious Disease, and Rhonda G. Kost, co-director of community-engaged research and clinical research officer of The Rockefeller University Hospital.

"This is an innovative, patient-centered project to determine the best method

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Memorial Sloan-Kettering Cancer Center, The Rockefeller University and Weill Cornell Medical College Form Pioneering Tri-Institutional Therapeutics Discovery Institute, Inc. (Tri-I TDI)

By Michael Foley

Michael Foley, Ph.D., Sanders Director of Tri-I TDI

In October of 2013, Memorial Sloan-Kettering Cancer Center, The Rockefeller University and Weill Cornell Medical College formed the pioneering Tri-Institutional Therapeutics Discovery Institute, Inc. (Tri-I TDI) and partnered with Takeda Pharmaceutical Company, Ltd, to expedite early-stage drug discovery leads to novel therapeutics that will impact human health. The TDI is funded, in part, by a generous $15 million gift from Lewis and Ali Sanders.

The TDI is a novel organization, governed by its own Board of Directors drawn from the Leadership of the three parent institutes. Its mission is to effectively develop therapeutics that arise from discoveries made in basic science labs. Its focus is on the early stages of developing compounds that make possible all-important "proof of concept" studies – those that increase the likelihood that targeting a specific biologic pathway can favorably alter the course of a disease.

Takeda Pharmaceuticals, a global research-based pharmaceutical company with a strong record of bringing new medicines to market is a close collaborator in this effort. Takeda provides 16 highly trained medicinal chemists who work on TDI projects in close collaboration with the project PI's and their lab members. These chemists are fully embedded in the Tri-I community and work in TDI's labs in the Belfer Research Building. In addition to these on-site chemists, the TDI also has access to other Takeda resources, such as structural biology capabilities, ADME/tox determinations, and virtual screening services through its groups located in Shonan, Japan, San Diego, CA and Boston, MA.

At present, there are seven projects in the TDI portfolio. A Scientific Advisory Board made up of experts in biology, chemistry and drug discovery and development from academics and industry selected these from over 45 applicants. These projects span a wide swath of the therapeutic spectrum, from oncology and psychiatric disease to rare diseases. Wet chemistry work on these projects began in July of 2014 and they are making swift progress.

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C. David Allis Wins the 2015 Breakthrough Prize in Life Sciences

By Zach Veilleux

C. David Allis, Ph.D.

For his foundational research on the unexpected regulation of gene activation by modifications to proteins that package DNA, work with implications for many diseases including cancer, Rockefeller's C. David Allis has been honored with the 2015 Breakthrough Prize in Life Sciences. Allis, Joy and Jack Fishman Professor and head of the Laboratory of Chromatin Biology and Epigenetics, was one of six life scientists to receive the prize at a gala awards ceremony in November 2014 at NASA's Ames Research Center in Mountain View, California.

Launched in 2013 by a group of Internet and technology entrepreneurs, the prize recognizes "transformative advances toward understanding living systems and extending human life."

A $3-million cash award accompanies the Breakthrough Prize, making it the richest prize in the life sciences, roughly double the Nobel Prize.

The founders are Google's Sergey Brin and Anne Wojcicki, Facebook's Mark Zuckerberg and Priscilla Chan, Yuri and Julia Milner, and Alibaba's Jack Ma and Cathy Zhang. Seth MacFarlane, executive producer of the 2014 television series Cosmos, hosted the award ceremony, which also featured the actors Kate Beckinsale, Benedict Cumberbatch, Cameron Diaz, Jon Hamm and Eddie Redmayne as presenters.

"Through his work on histone modifications, David has opened new doors of scientific understanding for colleagues around the world interested in penetrating the complexities of gene expression," says Marc Tessier-Lavigne, Rockefeller president, Carson Family Professor, and head of the Laboratory of Brain Development and Repair. "The Breakthrough Prize is a wonderful confirmation of the impact of his truly pathbreaking research."

The judges recognized Allis "for the discovery of covalent modifications of histone proteins and their critical roles in the regulation of gene expression and chromatin organization, advancing the understanding of diseases ranging from birth defects to cancer." Histones are DNA-packaging proteins, one component of chromatin, the material of which chromosomes are composed.

Over the last decade, Allis and others have provided evidence that suggests that patterns or combinations of chemical modifications to histones represent a layer of gene regulation that takes place away from the DNA, an epigenetic layer of regulation. Epigenetic errors have been associated with cancer and other diseases, and scientists' growing understanding of the fundamental mechanisms involved holds great promise for entirely new treatment approaches. Histone modifications have also been found to play an important role in cell reprogramming and are expected to contribute to the field of regenerative medicine.

"Tracking down answers to these fundamental questions concerning gene regulation has been deeply satisfying. More recently, too, we've seen that some of our findings are leading to new treatment

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Jeffrey Ravetch Wins Wolf Prize in Medicine

By Wynne Parry

Jeffrey Ravetch, M.D., Ph.D.

Jeffrey V. Ravetch, head of the Leonard Wagner Laboratory of Molecular Genetics and Immunology at Rockefeller University, was named a recipient of the 2015 Wolf Prize in Medicine. He shares the prize, which includes a monetary award of $100,000, with two other immunologists, Drs. John Kappler and Philippa Marrack. Kappler and Marrack work together at National Jewish Health in Denver, and Marrack is a member of Rockefeller's Committee on Scientific Affairs.

Since 1978, the Wolf Foundation in Israel has awarded annual prizes in the arts and sciences, which are presented by the President of Israel. This year, five prizes were presented to seven scientists and two musicians. The three winners of the medicine prize were selected for their work on the molecular basis of the immune response.

Ravetch dissects the cellular and molecular mechanisms that govern the generation of antibody specificity and the translation of that specificity into cellular responses. By identifying the genetic components that cause immune system cells to respond to specific antibodies, Dr. Ravetch hopes to gain a better understanding of how a functioning immune system protects organisms from invaders, and how a dysfunctional immune system attacks the body's own tissues.

Ravetch's award recognizes his studies of the "heterogeneous effector function of antibody molecules and his documentation of the importance of diverse receptors for the constant 'Fc' part of antibody molecules." Ravetch has studied in great detail the Fc region of many antibodies, and has showed that they are important in mediating antibody function both in pathogenic disease and the body's normal state.

"Jeff's work on Fc receptors has revealed critical knowledge of the molecular biology that underlies the immune system," says Marc Tessier-Lavigne, the university's president. "By showing how antibodies communicate chemically with immune system cells, his research is of great importance to the fight against both pathogenic disease and autoimmune disorders. It is gratifying to see his pioneering work recognized with this prestigious international award."

Ravetch graduated from Yale University in 1973 and entered the Rockefeller University-Cornell University M.D.-Ph.D. program. He received his Ph.D. in 1978 from The Rockefeller University, where he studied under Norton Zinder and Peter Model and his M.D. from Cornell University Medical College in 1979.

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Leslie Vosshall and Jean-Laurent Casanova Elected to the National Academy of Sciences

By Wynne Parry

Two Rockefeller scientists have been elected to the National Academy of Sciences. Leslie B. Vosshall, Robin Chemers Neustein Professor and head of the Laboratory of Neurogenetics and Behavior, has been named a member, and Jean-Laurent Casanova, senior attending physician, professor, and head of the St. Giles Laboratory of Human Genetics of Infectious Diseases, has been named a foreign associate. They are among 84 new national and 21 new foreign members.

Established by an act of Congress, the Academy provides independent, objective advice to the federal government and other organizations on matters related to health, science, and technology. New members are elected by their peers based upon their distinguished and continuing achievements in original research.

In addition to their appointments at Rockefeller, both Vosshall and Casanova are investigators with the Howard Hughes Medical Institute.

Jean-Laurent Casanova, M.D., Ph.D.

Casanova seeks to identify single-gene mutations responsible for "holes" in the immune defenses of otherwise healthy children, rendering them highly susceptible to specific infectious diseases.

Leslie Vosshall., Ph.D.

Vosshall works with flies, mosquitos, and humans to study how complex behaviors are controlled by cues from the environment and modulated by an organism's internal physiological state.

The Robertson Therapeutic Development Fund: Providing Critical Support for Translational Science at The Rockefeller University

By Bruce Conway

Robertson Therapeutic Development Fund Awards (May 2015)

Proof-of- Concept Awards*		
	Pilot	Advanced
	< $50 K	$50-300 K
Jan 2014	17	4
July 2014	11	4
Jan 2015	10	8
Total	38	16

*Full or Partial Funding received

Robertson Therapeutic Development Fund Awards (May 2015)

Early Clinical Development Awards	
	Title
May 2014	Agonistic anti-CD40 therapy enhanced by Fc gamma RIIB-targeted Fc-engineering
May 2014	Production of monoclonal Antibody 10-1074v for clinical study use and a phase 1 open label, dose-escalation study of the safety, pharmacokinetics and antiretroviral activity of 101074v mAb in HIV-infected and HIV-uninfected volunteers

The Robertson Therapeutic Development Fund (RTDF) was created in early 2014 to provide Rockefeller scientists with the resources required to advance promising basic research projects through the steps that lead to breakthrough medications, new diagnostic tests, or other clinical innovations. The grants, totaling $25 million over 5 years are provided by the Robertson Foundation.

One year after the successful launch of the RTDF, the initiative continues to provide the necessary resources to enable Rockefeller researchers to pursue important studies that are rarely supported by conventional funding mechanisms. In addition to funding support, the application and peer-review processes afford researchers an opportunity to learn best practices and considerations relevant for drug discovery and development programs from industry experts.

Two types of awards have been established through the RTDF. Proof-of-Concept Awards support early-stage projects aimed at identifying and validating potential therapeutic targets and diagnostics. Early Clinical Development Awards are intended to fund IND-enabling studies such as manufacturing and toxicology testing, and, in some cases, Phase I clinical trials. As such, these projects require larger grants with a longer duration.

To date, three cycles of funding for the Proof-of-Concept awards have been completed. For each round, a request for proposals (RFP) was distributed and an external panel of biotechnology and pharmaceutical experts and life sciences investment professionals was convened for proposal reviews. Recommendations to fund, in full or in part, or to withhold funding were made by the panelists. In the case of requests greater than $50,000, panelists had the option of requesting a more detailed and comprehensive Advanced Proposal. These proposals were subsequently sent for review by an external panel and scored according to the standard NIH scale.

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Meet the Scholar: Peter Forgacs, MD

By Michelle Romanick

Peter Forgacs, M.D.

Dr. Peter Forgacs joined the Clinical Scholars Program at the Rockefeller University in 2012. Dr. Forgacs received his M.D. from the Faculty of Medicine, University of Szeged in Hungary, and he joined Dr. Donald Pfaff's Laboratory of Neurobiology and Behavior as an Instructor in Clinical Investigation after completing his neurology residency at New York Presbyterian Hospital. Dr. Forgacs is also in Dr. Nicolas Schiff's Laboratory at Weill Cornell Medical Center.

Dr. Forgacs began his research career while in medical school where he joined the Brain Circulation Lab in the Department of Physiology and conducted studies on newborn piglets as a model for hypoxic brain injury in newborns. He presented the result of his research at student scientific meetings both locally and nationally.

Dr. Forgacs was interviewed by Dr. Nicolas Schiff for the Neurology Residency at Cornell and immediately became interested in Dr. Schiff's research on neurophysiological mechanisms of arousal and forebrain integration as well as clinical studies of the pathophysiology of impaired consciousness. Dr. Forgacs was excited about the approach and methods Dr. Schiff was bringing to understand brain functions in patients with severe brain injury and the concepts of how consciousness recovers after brain injury. Dr. Forgacs began to work in Dr. Schiff's laboratory during his residency and returned to New York to join his lab full time after finishing his Clinical Neurophysiology/Epilepsy Fellowship at Brigham and Women's Hospital, Harvard Medical School in Boston.

Dr. Forgacs' research involves patients who have history of severe brain injury and remain in states that are collectively known as "disorders of consciousness." These syndromes include coma, a condition typically seen in the first few weeks after injury when the patient is not responsive and their eyes are closed at all times; vegetative state, which is a condition distinguished from coma by intermittent eye opening despite total unresponsiveness; and the minimally conscious state, which is characterized by intermittent, but non-consistent responses to external stimuli. The prognosis of individual patients in the minimally conscious state is difficult to predict and the brain circuits involved in recovery are not well understood.

Several recent landmark observational studies Dr. Schiff's group have demonstrated that some such patients may recover after surprisingly prolonged periods of time following their brain injuries, even decades later. Thus, the main goal of Dr. Schiff lab's research is to improve our understanding of the underlying biological mechanisms in the recovery processes of consciousness in the severely injured brain and develop specific therapeutic interventions to improve recovery. An additional focus of Dr. Forgacs' research is to apply research concepts and methods to patients who are in Intensive Care Units (ICUs) after cardiac arrest. Many of these patients now receive therapeutic cooling, which improves outcomes and survival, but make it even more difficult to predict which patients will recover consciousness. Therefore better methods are needed to understand how to measure the integrity of specific brain regions that support consciousness recovery and to correlate these measurements with outcomes.

Dr. Forgacs had four specific expectations from the Clinical Scholars Program: 1) To further advance his career as a physician-scientist by providing educational activities related to conducting clinically-relevant research projects involving human subjects; 2) To experience positive examples of other physician-scientists who have successfully built research programs as physicians; 3) To provide ample 'protected time' to experience the full depth of conducting research and to be in the position to apply for independent support; 4) To have a community of physician-scientists with similar goals and interests. Dr. Forgacs stated, "All of these expectations were fully met and in many regards they exceeded my expectations."

When asked about his experience in the Clinical Scholars Program and his future plans, Dr. Forgacs responded with the following:

"Obviously there were plenty of learning opportunities, mostly from the leaders of the program and from my peer Clinical Scholars. Also, there is a very positive environment in the hospital, where research facilitators and nurses want to learn more about the scientific and medical importance of our study. I had many opportunities to explain our research in depth to many people who are involved.

Most surprising is how much I learned from other physician-scientists who are not working in the same field as I am. There are many common aspects of conducting research regardless of the specific topic and having many different ways of thinking about a problem actually broadens and improves the way I think about my own research. Without question, the most educational aspect is the remarkable insight and opinions about many different topics from Dr. Coller. The program provides an ideal environment, resources and educational program for clinicians who want to be physician-scientists combined with unparalleled intellectual inspiration from being part of the Rockefeller Community.

I plan to continue to work with Drs. Schiff and Pfaff and conduct research at Rockefeller University Hospital. My goal is the same as it has been since medical school – to be an excellent 'traditional' academic neurologist. I believe there is a great need for people like me, a physician who is a scientist (and vice versa) despite the increasing hurdles this choice for a career path involves."

The Rockefeller University Center for Basic and Translational Research on Disorders of the Digestive System Hosts First Gut Microbiome-Brain Interaction Symposium

By Daniel Mucida

The term microbiome was initially coined by Dr. Joshua Lederberg, former Rockefeller University President and 1958 Nobel laureate to define "the ecological community of commensal, symbiotic, and pathogenic microorganisms that literally share our body space".

Although the interest of the scientific community in the microbiome is thus not new, there has been a recent burst in microbiome research as a consequence of rapid advances in analytical and DNA sequencing tools to study microbial communities that inhabit our intestine.

The pioneering studies of the microbiome by Dr. Jeffrey Gordon and colleagues at Washington University have generated an increased interest in the possible role of the microbiome in different bodily functions. It is estimated that for each human cell, 10 bacterial cells occupy our body. Roughly 500–1,000 bacterial species exist in our microbiome, with enormous person-to-person variation. Importantly, different microbial composition between individuals or groups of individuals has been associated with susceptibility to several disease processes. In particular, research performed in recent years has demonstrated a clear impact of microbial colonization on the nervous system, sociability and the behavior of humans and model organisms.

Curious about these recent findings, Professors Torsten Wiesel and Bruce McEwen proposed hosting a symposium on the possible influence of the microbiome on different brain functions. On October 23, 2014, a very diverse set of nervous system investigators gathered at The Rockefeller University to discuss the current understanding of how gut microbes can influence central nervous system (CNS) development and behavior. Investigators from American, Canadian and European universities presented seven seminars on recent findings in both model organisms and humans.

Using DNA sequencing data from the gut microbiome, investigators including Drs. Jun Huh (University of Massachusetts), Emeran Mayer (UCLA) and Christopher Lowry (University of Colorado) showed correlations between gut microbial colonization and brain development and behavior. Dr. Jane Foster from McMaster University described recent findings linking anxiolytic behavior and reduced microbiota. Dr. Tracy Bale from the University of Pennsylvania expanded this analysis to vertical transmission of maternal microbes to offspring, studying its consequences to the neurodevelopment of newborns.

Dr. Elaine Hsiao from the California Institution of Technology described a role for commensal bacteria in murine models of autism in which oral exposure to certain commensal bacteria improved several behavioral defects in mice subjected to maternal-induced activation (MIA), a model of autism-related disorders. While the careful observations made by the investigators demonstrated dramatic behavioral effects, very little is known about the mechanisms and specific mediators responsible for the beneficial or detrimental effects exerted by bacterial species or groups of bacteria in these models. For instance, it is possible that circulating microbiota-derived metabolites could directly influence the CNS, or alternatively, activation of the immune system, or additional indirect mediators could be responsible.

A recent study, also conducted by Dr. Hsiao and her group, may shed light on this question since they found that the gut microbiota plays an important role in the regulation of a major neurotransmitter, serotonin, and that this pathway could impact several aspects of host physiology. Additional mechanistic studies that better define mediators of the microbiota-brain interaction, as well as more precise identification of the bacterial species and host cell types involved in these interactions, are needed to further advance this very interesting interdisciplinary field of research.

The symposium raised a number of important and challenging questions and made clear the enormous potential of this novel area of brain research. One indication of the interest in this field comes from noting that more than 200 enthusiastic students, investigators, staff, and faculty attended the event. This augers well for many additional novel discoveries as this area of research blossoms.

Manish Ponda, M.D. Receives 2015 Clinical Scientist Development Award (CSDA) from the Doris Duke Charitable Foundation

By Michelle Romanick

Dr. Manish Ponda received the 2015 Clinical Scientist Development Award (CSDA) from the Doris Duke Charitable Foundation to support his research "Understanding the mechanisms behind the disparate actions of endogenous vitamin D vs. vitamin D supplements on the lipid metabolism: a rational step towards optimizing treatment of vitamin D deficiency."

The CSDA program is part of the Doris Duke Charitable Foundation strategy to develop careers of physician-scientists. It has supported 234 investigators in their transition to independent R01 grant funding since its establishment in 1998. The CSDA provides researchers with the protected time and resources necessary to build their future research programs. The 2015 Clinical Scientist Development Awards are scheduled to commence on July 1, 2015.

Ana Emiliano, M.D. Receives a KO8 Clinical Investigator Award

By Michelle Romanick

Dr. Ana Emiliano, former Clinical Scholar and member of the Rockefeller Early Phase Physician Scientists (REPPS), received an NIH funded Mentored Clinical Scientist Research Career Development Award (K08) in May. The K08 award provides five years of salary support, as well as funds for research-related costs, for an intensive, supervised research career development experience in translational research.

Dr. Emiliano's project is entitled 'Tracing the origins of sleeve gastrectomy's glycemic effects.' Her mentor is Dr. Jeffrey Friedman and Head of the Laboratory of Molecular Genetics. She is studying the molecular mechanism fascinating observation that sleeve gastrectomy rapidly leads to improvement of glucose homeostasis, before any meaningful weight loss. Dr. Emiliano hasa developed a A mouse model of sleeve gastrectomy and is using it in combination along with state-of-the-art molecular biology techniques.

Current evidence indicates that the surgery not only leads to mechanical alterations in the gastrointestinal tract, but also promotes molecular adaptations in brain regions associated with energy homeostasis, such as the hypothalamus and specific centers in the hindbrain. In her study, obese mice undergo sleeve gastrectomy and then changes in neuronal signaling in specific brain regions are analyzed. Her goal is to identify neuronal populations controlling glucose regulation and energy balance that are specifically recruited by sleeve gastrectomy. Dr. Emiiano is also studying novel monogenic causes of obesity

Ana Emiliano, M.D.

Robert B. Macarthur, New Director of Pharmacy

By Michelle Romanick

Robert B. Macarthur, PharmD

Robert B. Macarthur, PharmD, MS joined the Rockefeller University Hospital in May 2015 as the Director of Pharmacy. Dr. Macarthur received his BS in Pharmacy from Rutgers University, New Jersey, his PharmD from St. John's University, New York and MS in Biostatistics from Columbia University.

Since 1988, Dr. Macarthur has work within the interrelated fields of hospital pharmacy and drug development as a Pharmacy Director. Most recently he served as Vice President of Clinical Development at Pharmaceutics International, Inc. (Pii), an FDA licensed, contract drug manufacturing organization that operates under Good Manufacturing Practices (GMP), in Hunt Valley MD. Pii manufacturers both commercial and investigational drug products that are distributed to the US, Europe, and Asia.

Prior to his position at Pii, Dr. Macarthur directed the Research Pharmacy at Columbia University. He remains affiliated with Columbia as a lecturer in the Department of Biostatistics, and currently teaches a semester long graduate course entitled, "New Drug Development: A Regulatory Overview" as part of their Clinical Research Methods Track graduate program.

Pii is a drug manufacturing company, which produces oral, topical, and injectable products. Dr. Macarthur's primary task was to create a GMP compliant investigational drug packaging and distribution department, to produce drugs for clinical trials, which entailed working with formulation scientists, analytical chemists, investigators, statisticians, and others to devise formulation, packaging, labeling and blinding methods. Most often these studies require a comparison of a marketed drug product with both an active test product and a placebo. All three products need to be characterized, per GMP, for identity, purity, activity, and stability over time. Products also need to be packaged and labeled in an identical manner as well as blinded and randomized. When devising packaging plans, we would always consider ways to simplify product management for the clinical sites while promoting patient safety and compliance.

My second task involved planning and overseeing the clinical trials performed to support the company's own products, aimed at gaining FDA

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Beatrice Renfield Lectureship in Research Nursing

By Rita Devine

The Rockefeller University Hospital and The Heilbrunn Family Center for Research Nursing hosted the annual Beatrice Renfield Lecture in Research Nursing on March 3, 2015 in the Carson Family Auditorium. This year's speaker, Afaf Meleis, Ph.D., Dr.P.S. (hon), FAAN; Dean Emerita and Professor of Nursing and Sociology at the University of Pennsylvania School of Nursing presented "NextGen Health Care: The Stars are Aligned".

The presentation focused on the experiences of those most burdened by societal inequities, in particular women and first generation immigrants, who are at the highest risk for illness but often have the least access to proper health care. She emphasized the challenges faced by health care professionals who provide that care.

Dr. Meleis is a world renowned nurse scientist and medical sociologist. Her research has helped to advance knowledge in global health, women's health, culturally-competent practice, and the development of the nursing discipline. She is the author of more than 200 publications on these subjects and is the recipient of numerous national and international awards and honors, including the Egyptian Medal of Excellence and an Honorary Doctorate of medicine from Linkoping University, Sweden.

The lecture was attended by 98 guests, including nurses from the New York region and nursing students. In addition, many people viewed Dr. Meleis's presentation via webcast provided through the Clinical Directors Network (CDN). The webcast is available through the CDN website under the CCTS Webcast Series section.

Sue Widmann, New Director of Nursing and Patient Care Service

By Michelle Romanick

Sue Widmann, R.N., M.P.H.

Susan Widmann joined Rockefeller University Hospital as the Director of Nursing and Patient Care Services in May 2015. Ms. Widmann received her Baccalaureate Degree in Nursing from the University of Michigan and her Master's Degree in Public Health from Harvard School of Public Health.

Ms. Widmann was formerly at Children's Hospital of Wisconsin in Milwaukee as the Director of Quality and Patient Safety where her responsibilities included quality, patient safety, infection control, and regulatory compliance. She also created and implemented a strategic quality improvement plan for the organization, and served as a key member of the leadership team charged with implementing a system-wide electronic medical record system.

Prior to being the Director of Quality and Patient Safety, Ms. Widman was the Director of Ambulatory Service at Children's Hospital of Wisconsin, where she was responsible for 23 clinics at four geographic sites with 230 full time employees and an annual growth rate of 10%. A key success of that position was the design, planning, and project oversight for the organization's first major off-site medical office building. The 80,000 square foot building, dedicated to pediatric specialized services, including a full imaging suite, opened on time and under budget.

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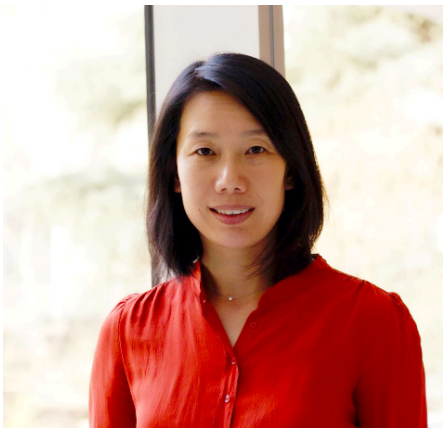
Yupu Liang, New Director of Research Bioinformatics in the Center for Clinical and Translational Science

By Michelle Romanick



Yupu Liang, Ph.D.

Dr. Yupu Liang was promoted to Director of Research Bioinformatics of the Center for Clinical and Translational Science (CCTS) on December 16, 2014. Dr. Liang received a Bachelor of Science degree in Biochemistry from the Nanjing University in 1998 and a PhD in Computer Science from the Graduate Center, City University of New York in 2014.

Prior to joining Rockefeller University, Dr. Liang was a senior bioinformatics engineer at Memorial Sloan-Kettering Cancer Center where she was responsible for developing analytical pipelines for both array and high throughput sequencing data. She also taught in the Tri-I Bioinformatics and Computational Workshops and collaborated with individual investigators on bioinformatics-related projects, including The Cancer Genome Atlas.

In her current leadership role, Dr. Liang oversees the bioinformatics support services of the CCTS. She has particular expertise in ontology-back human phenotyping projects, high-throughput DNA sequencing data analysis, RNA expression analyses, and bioinformatics education for Clinical Scholars and the wider Rockefeller University community. She leads the University's Bioinformatics/ Biostatistics Working Group, which includes many of the bioinformatics and biostatistics experts on campus. The Work Group's mission is to share research expertise, develop educational programs, and advise the University on strategic planning for bioinformatics resources.

When asked about future developments she envisions for the Research Bioinformatics program, Dr. Liang replied, "The next big project for the group is the development of a flexible platform that will enable phenotype recording, phenotype-genotype analysis, and user-friendly dynamic visualizations. We will also focus on state-of-art high-throughput sequencing analysis. Last but not least, we want to promote and develop the synergy between bioinformaticians and investigators."

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

By Michelle Romanick

On July 1, 2015, five new Clinical Scholars will join the Rockefeller University Clinical Scholars Program. They are: Drs. Kemal Akat, Patrick Brunner, Yehuda Cohen, Isaac Marin-Valencia, and Djin-Ye Oh. Additionally, with support from the CCTS, Benjamin Ungar, a 3rd year medical student from the Icahn School of Medicine at Mount Sinai in Dr. James Krueger's laboratory will continued in the Center's Year-Off Training Program for Graduate or Medical Students in Clinical and Translational Science, and with support from the Sackler Center for Biomedicine and Nutrition. Alexander Gomez, a 3rd medical student from the Icahn School of Medicine at Mount Sinai will join Dr. Paul Cohen's laboratory to study the role of thermogenic fat in mediating outcomes of bariatric surgery patients. Below are brief biographies and descriptions of research interests of the new scholars.

Kemal Akat, MD, PhD
Mentor: Dr. Thomas Tuschl
Laboratory: Laboratory of RNA Molecular Biology

Dr. Kemal Akat received his MD from the Faculty of Medicine, Heidelberg University and his PhD from the German Cancer Research Center in Heidelberg. He completed his Internal Medicine residency at the University Medical Center of the Johannes Gutenberg University Mainz and Postdoctoral Research Fellowship in the Laboratory of RNA Molecular Biology at The Rockefeller University. As a Clinical Scholar in Dr. Tuschl's laboratory, Dr. Akat is the role of RNA and RNA-regulatory proteins in the development of human diseases, especially cardiovascular disorders. He usese state-of-the art RNA-sequencing technologies to detect changes in gene expression and transcript processing in human clinical samples, and to define signatures of diagnostic or prognostic value. Animal models and basic RNA molecular biology supplement his studies on clinical samples to better understand disease mechanisms. A particular focus will be on cross-linking and immunoprecipitation (CLIP-sequencing) studies of RNA-binding proteins to identify targets and target sites of microRNAs and RNA-binding proteins.

Patrick Brunner, MD
Mentor: Dr. James Krueger
Laboratory: Laboratory of Investigative Dermatology

Dr. Patrick Brunner received his MD from the Medicine University of Vienna in Austria. He completed his Dermatology and Venereology residency at the Medical University of Vienna. As a Clinical Scholar in Dr. Krueger's laboratory, Dr. Brunner will study inflammatory skin diseases, including psoriasis and atopic dermatitis, and human mechanistic studies elucidating key pathophysiological steps in disease development and maintenance as a means to identify potential therapeutic targets.

Yehuda Cohen, MD
Mentor: Dr. Michel Nussenzweig
Laboratory: Laboratory of Molecular Immunology

Dr. Yehuda Cohen received his MD from Stony Brook University School of Medicine He completed his Internal Medicine residency at Montefiore Medical Center in New York and his Infectious Disease Fellowship at Beth Israel Deaconess Medical Center in Boston. Dr. Cohen will study novel strategies for the prevention and treatment of HIV infection, with a particular focus on candidate HIV vaccines and the use of broadly neutralizing monoclonal antibodies for the prevention and eradication of HIV infection.

Isaac Marin-Valencia, MD
Mentor: Dr. Joseph Gleeson
Laboratory: Laboratory of Pediatric Brain Disease

Dr. Isaac Marin-Valencia received his MD from the University of Las Palmas de Gran Canaria in the Canary Islands, Spain. He completed his Pediatric residency at the University of Barcelona and the University of Texas Southwestern Medical Center in Dallas, where he also completed his Pediatric Neurology residency. Dr. Marin-Valencia will study the cellular and molecular mechanisms of neurogenetic conditions in children, from structural defects to metabolic disorders that afflict the developing brain, with the goal of designing better diagnostic methods and therapies that can meaningfully improve children's wellbeing and psychomotor development.

Djin-Ye Oh, MD, PhD
Mentor: Dr. David Ho
Laboratory: Aaron Diamond AIDS Research Center

Dr. Djin-Ye Oh received her MD from Freie Universitaet and her PhD from Humboldt University in Berlin and Robert Koch-Institut in Berlin. She completed her Medical internship at Vivantes Auguste Viktoria Hospital and Microbiology residency at Charite University Medical Center in Berlin, Germany. She completed her Pediatric Infectious Diseases Fellowship at New York University Medical Center and Pediatric Infectious Diseases Research Fellowship at Boston Children's Hospital. Dr. Oh will study the molecular diversity of RNA viruses and the genetic and other mechanisms underlying the variation of the human immune response to viral infection, with the goal of developing novel approaches to prevent and treat HIV-disease.

Rockefeller University and Clinical Directors Network Share $2.8 million Award to Better Prevent Drug-Resistant Infections in the Community

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to prevent recurrence of community-acquired MRSA," says Barry Coller, director of the Center for Clinical and Translational Science and physician-in-chief of The Rockefeller University Hospital. "By focusing on what patients and clinicians identified as their highest priority in combating this disease, we are confident that we are devoting our scientific expertise to the community's major concern."

The PCORI award is among $102 million committed this fall to projects selected from among 409 proposals. Awards were made through a competitive review process by a committee composed of clinical scientists, patients, clinicians and other stakeholders.

"This project was selected for PCORI funding not only for its scientific merit and commitment to engaging patients and other stakeholders, but also for its potential to fill an important gap in our health knowledge and to give people information to help them weigh the effectiveness of their care options," said PCORI Executive Director Joe Selby.

"We look forward to following the study's progress and working with Clinical Directors Network and The Rockefeller University to share the results."

PCORI is an independent, nonprofit organization authorized by Congress in 2010 to fund patient-centered clinical comparative effectiveness research that will provide patients, their caregivers and clinicians with evidence-based information needed to make better-informed healthcare decisions. PCORI has approved $671 million to support 360 research studies and initiatives since it began funding research in 2012.

Memorial Sloan-Kettering Cancer Center, The Rockefeller University and Weill Cornell Medical College Form Pioneering Tri-Institutional Therapeutics Discovery Institute, Inc. (Tri-I TDI)

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from oncology and psychiatric disease to rare diseases. Wet chemistry work on these projects began in July of 2014 and they are making swift progress.

The Sanders Innovation and Education Initiative is a key component of the TDI. In partial fulfillment of this mission, the TDI launched the Tri-I TDI Sanders Seminar Series and hosted thought leaders in drug discovery and translational medicine, including Dr. Richard Lerner from Scripps Institute in San Diego and Dr. Joel Scherer from Lilly Chorus.

To bring innovative technology to the community, the TDI negotiated a groundbreaking deal with Schrödinger, the leading provider of high quality computational chemistry and biology software. This agreement provides free access to the full capabilities of this software package to the Tri-I community for 5 years. To ensure that users in the community are fully trained on the software and have the opportunity to take full advantage of its powerful capabilities, the TDI has hosted and will continue to host a series of training events lead by applications scientists from Schrödinger.

Over the next several months, the TDI will be expanding its mission into biologics and is preparing to support the discovery and development of therapeutic antibodies. The organization is recruiting an expert industrial partner in this area and is in the process of securing lab space and leadership for this new initiative.

As the Tri-I TDI continues to grow its capabilities in new and exciting ways, it will bring transformational change to the process of developing novel therapeutics on New York's Upper East Side.

C. David Allis Wins the 2015 Breakthrough Prize in Life Sciences

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approaches for difficult diseases," says Allis. "It is an amazing honor for this work to be recognized by such an extraordinary prize and it only increases my gratitude for the opportunity I've had to pursue a career in science."

Allis received his Ph.D. in 1978 from Indiana University and did postdoctoral work at the University of Rochester. He held academic positions at Baylor College of Medicine in Texas and at the University of Virginia before joining Rockefeller in 2003.

He is a member of the National Academy of Sciences and the American Academy of Arts and Sciences. He is the recipient of the 2011 Lewis S. Rosenstiel Award, the 2008 ASBMB-Merck Award, the 2007 Gairdner Award, the 2004 Wiley Prize, the 2003 Massry Prize, and the 2002 Dickson Prize in Biomedical Sciences.

As a winner of the Breakthrough Prize, Allis joins Rockefeller colleagues Cori Bargmann and Titia de Lange, who were among the inaugural group of prize awardees in 2013.

Jeffrey Ravetch Wins Wolf Prize in Medicine

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He completed his postdoctoral research at the National Institutes of Health with Dr. Philip Leder, where he cloned the immunoglobulin heavy chain genes and began his career-long interest in antibody function. In 1982 Ravetch joined the faculty of Memorial Sloan-Kettering Cancer Center and in 1984 also became a guest investigator in Rockefeller's Laboratory of Cellular Physiology and Immunology. He returned to Rockefeller in 1996 as professor and head of laboratory and was named Theresa and Eugene M. Lang Professor in 1997.

Ravetch's previous awards include the Canada Gairdner International Award in 2012, the Coley Award from the Cancer Research Institute in 2007, the American Association of Immunologists-Huang Foundation Meritorious Career Award in 2005, the Lee C. Howley Sr. Prize for Arthritis Research in 2004 and the Burroughs Wellcome Fund Award in Molecular Parasitology in 1986. He is a fellow of the American Academy of Arts and Sciences and the American Association for the Advancement of Science and a member of the National Academy of Sciences and the Institute of Medicine.

The Wolf Prize is considered one of the most prestigious prizes in medicine, along with the Nobel Prize, the Albert Lasker Award and the Canada Gairdner International Award. The previous Rockefeller recipient of the Wolf Prize in Medicine was Maclyn McCarty in 1990. Three Rockefeller faculty have been recipients of the Wolf Prize in Physics: Mitchell Feigenbaum and Albert Libchaber in 1986 and George Uhlenbeck in 1979.

The Robertson Therapeutic Development Fund: Providing Critical Support for Translational Science at The Rockefeller University

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As seen in the Table on page 3, a total of 54 Proof-of-Concept Awards have been approved for funding to date. Pilot grants were awarded for 38 projects that include 22 early-stage projects, 8 screens for therapeutic molecules, 4 novel diagnostic projects, 3 vaccine projects, and one cell therapy approach.

In addition, sixteen Advanced Proof-of-Concept (POC) grants were funded. The scope of funded Advanced POC projects covers a range of projects aimed at developing novel therapeutics, vaccines, biomarkers and medical devices.

In May, 2014, two Early Clinical Development Awards were also approved for funding; one for a novel anti-cancer therapeutic and one for the prevention of HIV infection.

Since the Fund's inception, RTDF has provided ~$10 million in awards to Rockefeller scientists. In total, 56 proposals submitted by researchers in 28 Rockefeller labs have received funding.

All Rockefeller Clinical Scholars, Postdoctoral fellows and research faculty are eligible for the awards, which are distributed according to a schedule based upon the successfull completion of agreed-upon milestones.

The Robertson Therapeutic Development Fund serves as a model for academic translational research initiatives and represents an important complement to the Tri-Institutional Therapeutics Discovery Institute (Tri-I TDI), a joint program with Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College designed to advance small molecule drug discovery programs. The RTDF supports projects in all stages of the drug development process as well as biological products and diagnostics that are not part of Tri-I TDI's current mission. In this way, the RTDF affords Rockefeller researchers an opportunity to leverage the most promising findings made in the University's labs to ultimately impact the patient. For more information on this exciting program, please contact Dr. Bruce Conway at 212-327-8376.

Featured RTDF Projects

Dr. Marina Caskey (Nussenzweig Lab) Early Clinical Development Award: P*roduction of monoclonal Antibody 10-1074v for clinical study use and a phase 1 open label, dose-escalation study of the safety, pharmacokinetics and antiretroviral activity of 101074v mAb in HIV-infected and HIV-uninfected volunteers.*

The Robertson Foundation has provided key support for Marina Caskey MD as an investigator and her efforts to advance highly neutralizing monoclonal antibodies against HIV-1 from the laboratory to the Clinic at the Rockefeller University Hospital. The flexibility and forward looking nature of the RTDF support has allowed Dr. Caskey, working with Drs. Michel Nussenzweig and Sarah Schlesinger, to bring 3BNC117, a new generation of broadly neutralizing antibodies, into the clinic in an expeditious manner. 3BN117 targets the CD4 binding site of the HIV envelope, and the CD4 receptor is the primary site of attachment of HIV to host cells, 3BNC117 shows activity against 195 out of 237 HIV strains.

Dr. Caskey's work was recently reported in the journal Nature (Nature online: April 8, 2015) and demonstrates that the experimental therapy can dramatically reduce the amount of virus present in patient's blood. This important observation, brings fresh optimism to the field of HIV immunotherapy and suggests new strategies for fighting or even preventing HIV infection. With continuing support from the RTDF, Dr. Caskey and the Zanvil Cohn Clinical Vaccine Center team are working to bring the next highly neutralizing monoclonal antibody, 10-1074, into the clinic.

Dr. Manish Ponda (Breslow Lab) Proof-of-Concept Award: Inhibition Factor XII: targeting a nov*el mechanism of inflammation in immune-mediated disease.*

"I joined Rockefeller as a Clinical Scholar to understand why kidney disease accelerates atherosclerosis. Encouraged to "follow the science", our work identified a novel role for coagulation factor XII (FXII) in immune cell migration, and we began to appreciate the potential role of FXII in immune-mediated disease. There are no FXII inhibitors available for clinical use, and transitioning from experimental science to drug development is high risk and often beyond the scope of traditional funding mechanisms.

The RTDF has proven to be an invaluable catalyst for accelerating the development of our FXII inhibitor technology. Furthermore, as a physician-scientist, advancing a basic science discovery into the pipeline of therapeutic development is intensely gratifying. With Bruce's help, we've built a team of experienced consultants and veteran medicinal chemists to take us through lead identification and optimization. The RTDF has effectively transformed the lack of a factor XII inhibitor from a barrier into an incredible opportunity."

Robert B. Macarthur, New Director of Pharmacy

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drug approvals. This task involved establishing a regulatory strategy and drug development pathway, guided by literature, FDA guidance documents, FOI information requests, and other sources.

The Pharmacy at Rockefeller University has heretofore been managed by New York Presbyterian Hospital (NYPH). Moving forward Dr. Macarthur will be establishing a pharmacy that is a department within Rockefeller University. His primary responsibilities involve overseeing the development of the Rockefeller University Pharmacy thru its transition from NYPH. As Pharmacy Director, additional responsibilities include maintaining safe dispensing practices, serving patients and research staff, and ensuring ongoing compliance with state and federal laws, and accreditation agency requirements. Dr. Macarthur will also be supporting the overall clinical research program at Rockefeller via participation in the Navigation Program and the Institutional Review Board.

When asked what is his vision and plans for the Pharmacy Department, Dr. Macarthur responded,

"NYPH has done a great job over many years at Rockefeller University, and I look forward to both continuing and building on that tradition. The clinical trials performed at Rockefeller bridge fundamental science with research on human disease. I expect the Rockefeller Pharmacy Service to contribute to that effort via the thoughtful application of pharmacy practice, and regulatory science. We live in a time where the drug development paradigm is rapidly changing, incorporating both large ("blockbuster") and small (orphan diseases and personalized medicine) population therapeutics. I intend to develop a pharmacy program at Rockefeller that will maximally support Investigators to accomplish both their study objectives, and, where appropriate, their goals to move products further down the "critical path" toward drug regulatory approval. The objective of all of this being to get novel, safe and effective medications to patients, faster."

Sue Widmann, New Director of Nursing and Patient Care Service

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When asked what her vision and future plans for the nursing department, Ms. Widmann replied, "Our goal is to insure that as clinicians we promote a safe and effective environment that actively supports clinical care. Nursing will effectively partner with the full research team to support the research process and insure good clinical practice. We will provide compassionate, safe, and patient-centered care while maintaining clinical research standards."

We welcome Ms. Widman to The Rockefeller University Hospital clinical community.

Masterminding Bacterial Classification - Centennial Vignette

By Elizabeth (Betsy) Hanson

Lancefield, Rebecca
Courtesy of the Rockefeller Archive Center

When Rebecca Lancefield (1895-1981) began studying the bacteria known as hemolytic streptococci, no one recognized that these microbes caused common—and dangerous—human diseases such as "strep throat," scarlet fever, rheumatic fever, acute kidney disease, and impetigo. Beginning in 1918, and continuing over the course of six decades, Lancefield devised a system for classifying the dozens of types of streptococcal bacteria. This system, still in use today, laid the groundwork for understanding the clinical course of these diseases and how they are transmitted.

A turning point came in the mid-1920s when Lancefield recognized that streptococci carry a protein on their cell surface that is correlated with virulence. Lancefield called this the M protein, and classified types of streptococci based on variations in this protein, as determined by their reactions with different antisera. She also found that the M protein prevents human white blood cells from engulfing and destroying streptococci unless an antibody is present to neutralize this effect. This explained why repeated strep throats, for example, are so common in childhood—immunity to one streptococcus does not prevent infection with another type.

During World War II, Lancefield's laboratory became known as the "Scotland Yard of streptococcal mysteries," as she worked with the Naval Medical Center, the Army's Board for Investigation of Epidemic Diseases, and others to type bacterial cultures isolated from patients in military hospitals. The evidence from the thousands of cultures that she typed informed later studies on streptococcal epidemiology and the mechanism by which rheumatic fever develops after a streptococcal infection with scarlet fever. The data also led to a practical immediate recommendation for less crowded barracks to reduce the chance of infectious outbreaks.

Lancefield, Rebecca
Courtesy of the Rockefeller Archive Center

Rebecca Lancefield received the BA from Wellesley College (1916) and the PhD from Columbia University (1925). She began her work on hemolytic streptococci in the laboratory of Oswald T. Avery in 1918. She left the next year, after Avery's project was completed, but returned to the Rockefeller Hospital in 1922 as an assistant in the laboratory of Homer Swift. She remained at Rockefeller for the rest of her career, rising to the title of professor in 1958. Lancefield served as president of the Society of American Bacteriologists and of the American Association of Immunologists. She was elected to the U.S. National Academy of Sciences, and her work was recognized by, among other awards and honorary degrees, the American Heart Association Achievement Award.