November 2011

The Rockefeller University Hospital
Center for Clinical and Translational Science
e-NEWSLETTER

Center News

Ralph Steinman (1943 – 2011) honored with 2011 Nobel Prize for discovering dendritic cells, sentinels of the immune system, and translating the discovery into improved therapies

Rockefeller University cell biologist Dr. Ralph M. Steinman, who discovered the immune system's sentinel dendritic cells and demonstrated that science can fruitfully harness the power of these cells and other components of the immune system to curb infections and other communicable diseases, is one of this year's recipients of the Nobel Prize in Physiology or Medicine. Dr. Steinman was awarded one half of the prize and the other is shared by Bruce A. Beutler of the University of Texas Southwestern Medical Center in Dallas and the Scripps Research Institute in San Diego and Dr. Jules A. Hoffmann of Institut de Biologie Moléculaire et Cellulaire, Université Louis Pasteur de Strasbourg

Dr. Steinman passed away on September 30. He was 68. He was diagnosed with pancreatic cancer four years ago and his life was extended using a combination of surgery, standard chemotherapy and experimental dendritic-cell based immunotherapy of his own design. When an infectious agent enters the human body, the immune system responds to get rid of it. But how does the immune response get started? That was the question that intrigued Dr. Steinman when he joined the Rockefeller laboratory of Zanvil A. Cohn (1926-1993) in 1970. It led him to discover a new type of immune system cell—the dendritic cell.

Dr. Steinman soon established that dendritic cells are the sentinel cells of the immune system, initiating the immune response. Subsequent research has revealed their complex roles: dendritic cells are now known to orchestrate the interactions of more than a dozen types of immune system cells, and they also play a role in preventing the immune system from attacking the body's own tissues. Understanding the basic biology of dendritic cells is leading to ways to harness them therapeutically in treating cancer and autoimmune diseases, and in developing new vaccines.

Drs. Steinman and Cohn began by studying cultures of cells called

Dr. Ralph Steinman

macrophages, which were known to be important in the immune response. When these experiments proved disappointing, Dr. Steinman decided to take another tack. Other investigators had shown that an immune response could be stimulated in a mixture of T cells, B cells, and unknown "accessory" cells harvested from mouse spleen. When he looked closely at the accessory cells

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Dr. Michelle Lowes, Clinical Scholars Program alumni, Receives RO1 Grant

By Michelle Romanick

Dr. Michelle Lowes, a graduate of the Clinical Scholars Program and an Assistant Professor of Clinical Investigation in the Laboratory for Investigative Dermatology, recently received a 3 year independent investigator RO1 grant from the NIAMS branch of the National Institutes of Health entitled 'Origin and Function of Inflammatory Dendritic Cells in Psoriasis.' Dr. Lowes is currently a member of the Rockefeller Early Phase Physician Scientists (REPPS) (http://repps.rockefeller.edu/) and an alumnus of the Clinical Scholars Program.

Dr. Lowes's broad research area is skin immunology, with a "dendritic cell-centric" focus. The classic functions of dendritic cells (DCs) are to sense "danger", migrate to local lymph nodes, and present antigen for T cell activation and adaptive immunity. The skin disease psoriasis is an ideal model to study DCs because they accumulate in psoriatic inflammatory lesions, and they are readily accessible in skin samples of involved areas making it possible to study the impact of novel agents that modulate disease activity.

Dr. Lowes has developed and refined techniques to phenotype, localize, isolate, and study both DC and T cells from healthy and diseased human skin. The lab first described a population of "inflammatory" myeloid DCs, which are as abundant as T cells in psoriasis skin lesions. These inflammatory DCs were reduced with every treatment for psoriasis examined, but not decreased if the treatment did not improve the psoriasis.

The central hypothesis of Dr. Lowes's is that circulating CD16+ monocytes are

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Finding Out What Research Volunteers Really Think About Participating in Research

By Rhonda G. Kost

Surprisingly, in the otherwise data-rich environment of translational research, we know very little about what research participants think about their research experiences. Three decades of research into the design and use of patient-centered surveys to assess the hospital care experience-- now routinely required by federal funding agencies and accrediting agencies—has demonstrated that collecting and analyzing patient perceptions improves patient care and clinical outcomes, and reveals unexpected patient priorities and perceptions.

Applying similar rigorous methodology to understand research participants' perceptions has the potential to: identify motivations to participate in research protocols, assess how well the informed consent procedure prepare participants for their actual research experiences; provide information on the quality of the participants' experience, including their interactions with the research team, and provide data to improve participant recruitment, the research experience, and the provision of ethical protections.

Under the leadership of Dr. Rhonda, Kost, the multi-center Research Participant Perception Survey Project, a collaboration between the Rockefeller Center for Clinical and Translational Science (CCTS) and the NIH Clinical Center, has made significant progress, including the creation and initial fielding of a validated questionnaire to measure research participant experiences.

Supported by the Rockefeller CTSA grant, the project is designed to find out how participants view their experiences in clinical research, provide national benchmarks for the conduct of clinical research, and generate data for evidence-based performance improvement of human research protections and research conduct. The initial phase focused on using rigorous qualitative methods to define the aspects of research participation that are important to research participants so as to inform the creation of a questionnaire.

The second phase was designed validate the questionnaire, obtain national benchmarks for performance, and provide local performance data to clinical research centers. A paper describing the results of the initial phase, including the results of 18 focus groups of participants and research professionals that were conducted at 8 academic research centers, was recently accepted for publication (Kost, et al.; CTS 2011, in press). In brief, research participants most commonly rated altruism, access to treatment, and learning about health as important factors in joining research projects; of particular note, financial compensation was rated a less important motivation to join or stay in a research study than many professionals predicted.

Participants varied widely in the way they reacted to potential risks of participation and other study details, but almost universally participants rated being treated with respect by the research team as essential to a positive experience. Reinforcing this last theme was the finding that when participants felt that they were not being treated with respect, they were likely to decline to participate or leave a protocol before it ended.

Survey questions were developed based on data from the focus group work. The questions spanned the entire process of research participation, from initial recruitment, through enrollment and study conduct, to completion or withdrawal.

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Dr. Diane Maydick, New Director of Nursing and Patient Care Services

By Michelle Romanick

Diane Maydick, EdD, RN joined the Center on October 31, 2011 as Director of Nursing and Patient Care Services. Dr. Maydick has been a nurse for more than thirty-five years and has worked in a variety of settings including tertiary care medical centers in the New York Metropolitan area, home health care, and the medical device industry. She has spent many years as a Wound, Ostomy, and Continence (WOC) Nurse Specialist. Dr. Maydick serves as Chairperson of the Marketing and Communications Committee for the WOCN® Society, is a reviewer for the society's journals, and serves on the editorial review board for Ostomy/Wound Management.

Throughout her career Dr. Maydick has mentored numerous students and colleagues. She continues to lecture on topics related to wound care, pressure ulcer prevention and treatment, ostomy care, and nursing outcomes, as well as her experiences in acute care, rehabilitation and outpatient settings. Dr. Maydick has served as a preceptor to numerous WOCN and Master's level students. Additionally, she has worked with industry partners, providing assistance with education, research, and publications.

Dr. Maydick received her BS in Nursing from Rutgers, The State University of New Jersey, an MS in Nursing from Hunter College, The City University of New York, and an EdD in Organizational Leadership and Development- in the Nurse Executive Program at Teachers College, Columbia University. Her recent research included investigating quality of life for individuals with a permanent ostomy. More specifically, the relationships of preoperative stoma site marking by an ostomy nurse, peristomal skin complications, and out -of -pocket costs for ostomy management and their relationships to quality of life were explored.

Dr. Maydick has held numerous positions in the New York Metropolitan area, most recent position was at New York Presbyterian/Weill Cornell as a Clinical Nurse Specialist in WOC Nursing. In this role she worked diligently to improve quality and patient outcomes across a variety of settings.

Dr. Maydick is a member of the Wound, Ostomy, and Continence Nurses Society, Sigma Theta Tau, and the Hunter College Alumni Association. She received an Excellence in Clinical Practice Award from Hunter College, and has presented her research locally and nationally, most recently at the WOCN National convention held in New Orleans in June, 2011.

Dr. Maydick stated, "I am delighted to be joining the Rockefeller University Hospital and look forward to using my extensive clinical, educational, and industry experiences in my new role as Director of Nursing and Patient Care Services."

New Clinical Scholars Join the Center for Clinical and Translational Science

By Michelle Romanick

On July 1, 2011, eight new Clinical Scholars joined the Rockefeller University Clinical Scholars Program. They are: Drs. Ana Emiliano, Thalia Farazi, Daniel Gareau, Sharon Karmon, Florian Klein, Ana Pereira, Jeremy Segal, and Ana Tuyama. Additionally, with support from the CCTS, Rachel Shively joined the Year-Off Training Program for Graduate or Medical Students in Clinical and Translational Science. Ms. Shively is spending her research year in the laboratory of Dr. Vincent Fischetti. Below are brief biographies and research interests of the new Scholars and medical student. Please join us in welcoming them.

Ana Emiliano, MD
aemiliano@rockefeller.edu
Mentor: Dr. Jeffrey Friedman

Dr. Ana Emiliano received her MD from Universidade Federal do Rio de Janeiro in Rio de Janeiro, Brazil. She completed her Internal Medicine and Psychiatry Residency at the University of Rochester, and her Endocrinology Fellowship at johns Hopkins University. As a Clinical Scholar in Dr. Friedman's lab, Dr. Emiliano will be studying the mechanisms leading to the development of leptin resistance and how to circumvent this problem in order to effectively treat obesity.

Thalia Farazi, MD, PhD
tfarazi@rockefeller.edu
Mentor: Dr. Thomas Tuschl

Dr. Thalia Farazi received her MD and PhD from Washington University School of Medicine. She completed her Pediatrics Residency at Boston Children's, and her pediatric hematology/oncology and neuro-oncology fellowship at Memorial Sloan Kettering Cancer Center. As a Clinical Scholar in Dr. Tuschl's lab, Dr. Farazi will study the role of post-transcriptional gene regulation in breast cancer. She is focusing on understanding the role of miRNAs and RNA binding proteins in tumorigenesis to identify diagnostic and prognostic markers, as well as define their regulated pathways

Daniel Gareau, PhD
dgareau@rockefeller.edu
Mentor: Dr. Jim Krueger

Dr. Dan Gareau received his PhD from Oregon Health Science University. He completed his post doc in Cancer Imaging at Memorial Sloan-Kettering Cancer Center and Oregon Health Science University. As a Clinical Scholar in Dr. Krueger's lab, Dr. Gareau will study biophotonics with an emphasis on novel spectroscopic and morphometric techniques for screening and characterizing skin cancer. Devices under development include a rapid confocal line-scanner for noninvasive, 3D, whole-lesion imaging with cellular resolution and a low-cost hyperspectral camera for enhanced dermoscopy. He is also developing software to automatically render quantitative pathometrics from the images.

Sharon Karmon, MD
skarmon@adarc.org
Mentor: Dr. Martin Markowitz

Dr. Sharon Karmon received her MD from Johns Hopkins School of Medicine and MPH from Johns Hopkins Bloomberg School of Public Health. She completed her Infectious Disease fellowship at New York University School of Medicine. As a Clinical Scholar in Dr. Markowitz's lab, Dr. Karmon will study transmitted HIV-1 drug resistance mutations and the role of ibalizumab, an anti-CD4 monoclonal antibody, in the treatment and prevention of HIV.

Florian Klein, MD
fklein@mail.rockefeller.edu
Mentor: Dr. Michel Nussenzweig

Dr. Florian Klein received his MD from the University of Cologne in Germany. He joined Dr. Michel Nussenzweig's Laboratory of Molecular Immunology after completing his residency in Internal Medicine at The University of Cologne. As a Clinical Scholar in Dr. Nussenzweig's lab., Dr. Klein will investigate the function of B lymphocytes and the development of antibodies in HIV-infected patients, in particular antibodies with broad neutralizing activity against HIV.

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New Rockefeller Bioinformatics/Biostatistics Collaborative Group Launched

By Edward Barbour

February 10th 2011 marked the first meeting of the campus-wide collaborative group for Bioinformatics and Biostatistics. Since the inaugural meeting, the group has assembled bimonthly for interesting presentations given by invited guest speakers and lively discussion on the relevant topic of the day. The groups' mission is to provide a platform where interested professionals can share new ideas and "problem solve" in a friendly collegial environment.

Even though it is a relatively new field, Bioinformatics' breadth, complexity, and rapid growth is extraordinary. As a result, it is timely to have a group of investigators on campus who share in the enthusiasm to use bioinformatics/biostatistics to unlock the mysteries of biological science. The group will also play a crucial role in planning for the "data tsunami" ensuing from the new generation of "omics" data. The groups' name reflects the need for seamless integration of Bioinformatics and Biostatistics to most effectively advance the scientific mission.

At the group's meeting on October 21st, Dr. Chaolin Zhang from the laboratory of Dr. Robert Darnell presented details of the bioinformatics processing involved in the HITS-CLIP techniques of Protein-RNA interaction analysis. CLIP stands for Cross Linking and ImmunoPrecipitation while HITS stands for HIgh Throughput Sequencing. This methodology has greatly improved our understanding of the role RNA binding proteins in biology and disease. The Darnell lab has studied the role of the Nova protein in alternative splicing and brain regulation by analyzing RNA sequences at single nucleotide resolution from RNA bound to the Nova protein. The presentation highlighted the novel bioinformatics/biostatistics methods developed and applied by Dr. Zhang.

The collaborative group's efforts are just beginning and they are expected to expand by exploring numerous 'cutting edge' bioinformatics and biostatistics techniques, algorithms, and applications to advance Rockefeller science.

All individuals on campus with an interest in bioinformatics or biostatistics are welcome to join the group. Please contact Ed Barbour at ebarbour@rockefeller.edu to be added to the list of invitees for upcoming meetings.

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

By Michelle Romanick

The Rockefeller University Center for Clinical and Translational Science (CCTS) awarded 32 pilot projects this year, of which 10 are to CCTS Clinical Scholars. A record total of 44 applications were submitted and the scientific quality was truly outstanding. Reductions in the CTSA grant award limited the number of awards and the amount per award, with a total commitment of $ 454,746. This brings the grand total of pilot project funding to $1,622,434 since this program was begun under the initial CTSA grant in 2006. These pilot project awards will continue to support clinical and translational studies being conducted at The Rockefeller University.

Pilots Projects Led by CCTS Clinical Scholars

Niroshana Anandasabapathy, MD, PhD: *Use Of Flt3L to Help Phenotype and Characterize Human Cross-Presenting Dendritic Cells In Vivo.* This project will develop alternative approaches to vaccine design based on fundamental principles of immune memory, which include targeting vaccine antigens to specialized dendritic cell subsets.

Jennifer Belasco, MD: *Evaluation of the Role Of Dendritic Cells In Psoriatic Arthritis.* This project will determine whether myeloid dendritic cells (mDCs) and plasmacytoid dendritic cells (pDCs) are increased in peripheral blood, synovial tissue, and skin from subjects with psoriatic arthritis (PsA) as compared to synovial tissue of subjects with osteoarthritis and skin of normal controls. The project will also compare the production of dendritic cell-associated cytokines- IL12, IL10, IL6, and IFNa-present in the tissue of subjects with PsA with those inpatients with osteoarthritis and in normal controls. Analysis of the differences in gene expression patterns of dendritic cells from subjects with PsA normal controls and subjects with osteoarthritis will also be performed.

Iddo Ben-Dov, MD: *Urine miRNA in Autosomal Dominant Polycystic Kidney Disease*. The aim of this project is to assess the potential of urine miRNAs as biomarkers in autosomal dominant polycystic kidney disease. The project employs biochemical handling and computational analyses that have already been successfully applied to urine samples from healthy volunteers. A urine comparison of the miRNA profiles of twenty ADPKD patients will be made with twenty CKD control patients. The main expected result is the generation of variability statistics that will serve to guide the design of larger-scale biomarker studies.

Ana Emiliano, MD: *Effects of Metabolic States on Anxiety Responses in Normal Body Weight and Obesity.* In this project, patients will be presented with the threat of shock paradigm while in either a fed state or fasted state. fMRI data as well as self-reported measures and analyses of stress hormones will be made between groups to address whether the perception of stress and its markers and/or the fMRI response is altered by food restriction.

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21 Graduate from the Center for Clinical and Translational Science Certificate Program

By Michelle Romanick

On June 3, 2011, 21 participants from across campus graduated from the Center for Clinical and Translational Science Certificate Course, having completed two courses over the academic year. The defining feature of the course is the requirement that each student creates her or his own hypothetical human subjects protocol, including an informed consent form. The students learn about each element of the protocol development and how it connects to the protocol development and review process through a series of tutorials in which outstanding translational investigators describe their research.

Structural Biology Class

After completing their protocols, the participants functioned as a mock IRB, reviewing each of the protocols and offering suggestions to insure the optimal design and the greatest protection of the human subjects for each study. The protocols that were submitted in fulfillment of the requirement of the course were of exceptionally high caliber and offered insights into the clinical research interests of the talented group of investigators who enrolled in the program.

The first course, Introduction to Clinical and Translational Science, was offered in fall 2010. The course was 12 weeks and consisted of two 90-minute lectures per week. The first lecture described an important element in clinical and translational science (e.g., biostatistical considerations, human subjects protection, study design, and conflict of interest), and the second lecture was a scientific presentation by a Rockefeller University investigator explaining her or his research, emphasizing the element taught at the beginning of the week. The second course in the program, Introduction to Scientific Techniques in Clinical and Translational Science, began in March 2011. Led by Drs. Sarah Schlesinger and James Krueger, the course introduced the students to core resources available at Rockefeller University and their application to address critical problems in human biology. The students learned from the Rockefeller University core resource leaders about the resources available, and how to apply them to their research. The final project of the course involved the students returning to the protocols they developed in the Introduction to Clinical and Translational Science course and enhancing them by adding new techniques such as bio-imagining, monoclonal antibodies, high throughput screening, or gene targeting that would augment the research design and facilitate their ability to test their hypotheses.

Both courses received high evaluation marks by the students, with 100% of the students reporting that they would recommend the courses to others, nearly 82% of the students stating the course changed their views about clinical and translational research, and approximately 94% of the students stating that the course made them more likely to conduct clinical or translational research.

Students' comments:

"It opened a totally different world."

"This was a fantastic course. I enjoyed the breadth of the class topics and the great guest lectures."

"This is a place where we can learn about all of the techniques and then we can think which is best for us."

The next Certificate Program will begin in the fall of 2012, and applications will be open December 2011.

2010 – 2011 Certificate Program Graduates

Hospital Safeguards Sensitive Information with New Software Tool

By Antonia Martinez

In September 2011, the hospital's senior staff started utilizing a new software tool to help ensure that sensitive information was not stored on unsecured hospital computer drives. Identity Finder, available for Mac and PC computers, scans hard drives, removable drives, and remote computers for social security, credit card, and bank account numbers, as well as other sensitive data that the user specifies. It automatically removes or protects data according to the user's settings. "Not that long ago, people wrote their social security numbers on everything, even grant applications and CV's", states Project Manager, Ross Gillman.

People are better informed now about the sensitivity of listing personal identifiers. Protecting this kind of information is a university policy, as well as New York State law. Identity Finder assists users to comply with both directives. Identity Finder was first introduced on campus in the fall of last year as part of Information Technology's strategic information security initiative.

Deployment of the software within labs and departments that handle sensitive data was a key element in a three-pronged approach to: identify and secure sensitive and confidential university data; protect data from unauthorized access; and to remove or encrypt files that may exist unsecured on desktops, laptops, handhelds, or other devices.

As a data owner or custodian of university data, the hospital (like all university labs and departments that handle sensitive data) is responsible for taking proactive measures to reduce the risk of loss or exposure of these data through theft, malware infections, and inadvertent online disclosure. "The focus now is on sensitive data," says Mr. Gillman about the hospital's implementation of Identity Finder. "In the future, we will also focus on data protected under the HIPPA statute. We will use Identity Finder to create custom dictionaries that can be used to find combinations of data that may contain Personally Identifiable Information (PII), such as patient names with addresses, for example. We have a legal duty to keep this information confidential.

Identity Finder allows us to perform our duty more efficiently." Identity Finder is available to Rockefeller labs and departments, as well as hospital staff. To learn more about the strategic security information initiative, visit the IT Web site at http://it.rockefeller.edu/index.php?page=infosec.strategic.initiative. For more information about Identity Finder, visit the IT Web site at http://it.rockefeller.edu/index.php?page=infosec.idfinder, or contact Ross Gillman at ext. 8930 to discuss deployment in your area.

Dr. Leanne Johnson-Huang awarded the Linda and Leonard Berkowitz post-doctoral fellowship

By Michelle Lowes

Leanne Johnson-Huang completed her Ph.D. in 2007 at the University of Pennsylvania, studying the role of cytokines in helper T cell differentiation during parasitic infections. However, her goal was to work in a translational setting, applying her skills to the study of human health and disease. Dr. Johnson-Huang is particularly interested in human cutaneous immunology, because investigators have direct access to skin tissue and can study immune responses within the skin with relative ease. She joined the Laboratory for Investigative Dermatology at The Rockefeller University early in 2008 as a post-doctoral associate.

Dr. Johnson-Huang is currently exploring the immune mechanisms that may regulate inflammation in psoriasis. Her recent studies have uncovered a potential anti-inflammatory pathway that fails to function in psoriasis. Dr. Johnson-Huang was awarded the Linda and Leonard Berkowitz post-doctoral fellowship in June 2011. This 12 month fellowship, made possible by the Mazer Foundation, will help facilitate her research into the role of cytokines in autoimmune inflammation in psoriasis. Knowledge of these anti-inflammatory pathways is not only crucial for the development of novel therapeutics, but can also be extended to the understanding of other autoimmune diseases, with the ultimate goal being to prevent inflammation.

Linda Berkowitz, Leonard Berkowitz, David Berkowitz, Michelle Lowes, and Leanne Johnson-Huang

Ralph Steinman (1943 – 2011) honored with 2011 Nobel Prize for discovering dendritic cells, sentinels of the immune system, and translating the discovery into improved therapies

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using phase-contrast light microscopy, he saw large cells with branch-like projections, which continually extended and retracted. He called them dendritic cells, after the Greek word for tree.

In the following years Steinman and colleagues characterized dendritic cells and proved their potency in initiating a T-cell response, a crucial step in the immune response. They also developed techniques to grow dendritic cells in culture rather than isolate them from mixtures of immune cells. Making cultured dendritic cells readily available for study opened the door to other researchers, and today hundreds of laboratories around the world devote their work to the basic biology and clinical applications of dendritic cells. Many groups are now using them as part of immune therapies for cancer. Dr. Steinman and his colleagues developed novel ways to target dendritic cells so as to enhance the response to vaccines to protect against HIV and other infectious diseases.

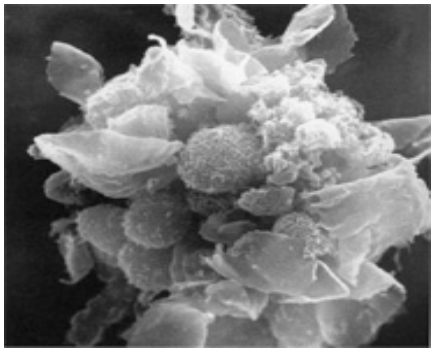

Image of the dendritic cell

Dr. Steinman was born in Montreal, Canada on January 14, 1943. He received a B.S. degree, with honors, from McGill University in 1963, and an M.D., magna cum laude, from Harvard Medical School in 1968.

After completing an internship and residency at Massachusetts General Hospital, he joined The Rockefeller University in 1970 as a postdoctoral fellow in the Laboratory of Cellular Physiology and Immunology headed by Cohn and the late James G. Hirsch. He was appointed an assistant professor in 1972, associate professor in 1976, and professor in 1988. He was named Henry G. Kunkel Professor in 1995, and director of the Christopher Browne Center for Immunology and Immune Diseases in 1998.

A recipient of the Freidrich-Sasse, Emil von Behring, and Robert Koch Prizes, Dr. Steinman also has received the Rudolf Virchow and Coley Medals and the Gairdner Foundation International Award. He was awarded honorary degrees from the University of Innsburck and Free University of Brussels. He also received the 2004 New York City Mayor's Award for Science and Technology, the 2007 Lasker Award for Basic Medical Research and the 2009 Albany Medical Center Prize in Medicine and Biomedical Research. He was a member of the U.S. National Academy of Sciences and its Institute of Medicine. A scientific symposium in honor of Steinman is being planned for the spring of 2012.

Dr. Michelle Lowes, Clinical Scholars Program alumna, Receives RO1 Grant

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recruited into the skin and become activated by the local environment to develop into inflammatory DCs. These monocytes migrate into the skin due to the chemotactic gradient of fractalkine. There are many examples of monocytes becoming inflammatory DCs and macrophages in murine models, including colitis, infections, atherosclerosis, and myocarditis.

Although much less in known in humans, circulating CD16+ monocytes are elevated in psoriasis and other conditions, including sepsis, rheumatoid arthritis, HIV infection, and coronary artery disease. The experiments in this project will directly enhance our knowledge of monocyte populations and the DCs and macrophages they give rise to, and support the development of new treatment protocols to target these cells in psoriasis and other autoimmune diseases.

Dr. Lowes obtained her medical degree from the University of New South Wales, Australia, and her PhD from the University of Sydney, Australia. She is a board-certified Dermatologist in Australia. Dr. Lowes came to Rockefeller University in 2001 when she joined the Clinical Scholars Program. She has been an NIH-funded investigator since 2006 and has also received funding from The Doris Duke Foundation, The Dana Foundation, and the Rockefeller University Clinical and Translational Science Award (CTSA).

Leanne Johnson-Huang, Tim Lentini, Michelle Lowes, Katherine Pierson

Finding Out What Research Volunteer Really Think About Participating in Research

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The questionnaire was finalized in collaboration with the NRC Picker company, a leader in the creation, validation, and analysis of hospital patients' surveys. The questionnaire was mailed to 18,980 research participants at 15 academic research institutions (including 13 CTSAs) across the country, and 4,961 responses (29%) were returned. Several methods were used to analyze both the validity of the questions and the five conceptual groupings of questions, namely, trust, informed consent, respect for patient preferences, information-education-communication, and coordination of care. Questionnaires were sent to more than 1200 Rockefeller participants, and 384 responded, split nearly evenly between healthy volunteers and participants with specific disorders.. The group responding included 15% Hispanic/Latino, 21% Black African-Americans, 72% Caucasians, and 8% Asians participants. Overall, participants were very positive about their experiences at Rockefeller. Thus, 79% rated their research experience as "Best' (9 – 10 on 0 – 10 scale), and 72% indicated they would recommend participation to their friends and family. A detailed analysis of all of the questions is currently underway and several manuscripts describing the results are in preparation. Future e-Newsletters will contain articles that provide detailed discussions of specific themes. NRC Picker will make the survey available as part of their survey offerings in early 2012. If it is adopted broadly, the survey has the potential to establish national standards and encourage data-driven performance improvement across CTSA institutions and beyond!

New Clinical Scholars Join the Center for Clinical and Translational Science

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Ana Pereira, MD
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Mentor: Dr. Bruce McEwen

Dr. Ana Pereira received her MD from the Universidade Federal de São Paulo in Brazil, trained in neurology at Harvard Medical School, and did her post doctoral training in the Taub Institute for Alzheimer's Disease at Columbia University Medical Center. As a Clinical Scholar in Dr. McEwen's lab, Dr. Pereira will study the glutamatergic excitotoxic events that occur in the brains of patients in the earliest stages of Alzheimer's disease with the use of advanced brain imaging techniques. She will also test potential therapeutic interventions that can retard the progression of the disease. In addition, Dr. Pereira will study the mechanisms of normal cognitive aging in rats and humans and the risk factors for pathological brain aging.

Jeremy Segal, MD, PhD
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Mentor: Dr. Elaine Fuchs

Dr. Jeremy Segal received his MD from Weill Cornell Medical Center and PhD from The Rockefeller University. He completed his Anatomic Pathology residency at New York Presbyterian Hospital and Molecular Genetic Fellowship at Hospital of the University of Pennsylvania. As a Clinical Scholar in Dr. Fuchs's lab, Dr. Segal will study the effect of aging on the skin from a stem cell perspective. Stem cells are the reservoir from which new mature cells originate when required for normal tissue homeostasis or the response to injury, and so it is important to determine how stem cells change with age and how these changes might underly the aged phenotype.

Ana C. Tuyama, MD
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Mentors: Drs. Jan Breslow and Edward

Dr. Ana Tuyama received her MD from the School of Medicine at the Federal University of Minas Gerais, in Brazil. She completed her Internship, Internal Medicine Residency and Fellowship in Gastroenterology and Hepatology at the Mount Sinai School of Medicine, New York. As a Clinical Scholar in the labs of Drs. Breslow and Fisher, Dr. Tuyama's research focuses on nutrition and metabolic diseases, including lipoprotein metabolism, obesity, and fatty liver disease. More specifically, she currently studies how the process of autophagy regulates VLDL metabolism.

Rachel Shively
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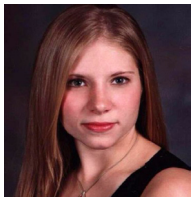
Mentor: Dr. Vincent Fischetti



Ms. Rachel Shively is currently a fourth year medical student at the Mount Sinai School of Medicine in the 2011 CCTS Year-Off Medical Student Training Program in the lab of Dr. Fischetti. Ms. Shively is spending a year helping to develop a vaccine against the Group A Streptococcus. The vaccine is a conjugate vaccine composed of the M protein conserved region and the Group A carbohydrate.

The Rockefeller University Library New PubSubmit System

By Maija Williams

The Rockefeller University has instituted a new PubSubmit system for investigators. This system makes obtaining a PMCID number for publications that are supported by NIH funded research easy. Investigators can now click on the PubSubmit system button on the library's webpage, submit their publication and the library will take care of the rest. Once a PMCID has been assigned the library will alert the investigator of their PMCID number. For more information and access to the PubSubmit system please visit https://it.rockefeller.edu/issnews/scientific/108.

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

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Thalia Farazi, MD, PhD: *Development of Multicolor Fluorescence RNA In Situ-Hybridization Assays For Breast Cancer Diagnosis and Prognosis.* This project will employ a novel mRNA multicolor direct in situ hybridization approach in analyzing breast tissues for three breast cancer diagnosis-related transcripts (ERBB2, ESR1 and PGR), as well as other potential RNA biomarkers, including non-coding RNAs.

Daniel Gareau, PhD: *Development of an Automated Bedside Confocal Morphometric Video-Microscopy Pathology.* The confocal microscope performs noninvasive "optical sectioning," as an alternative to invasive physical sectioning (biopsy/histology) to achieve similar cellular resolution. Melanosomes provide strong visual contrast to the relevant lesion morphology. Computer vision with automated pattern recognition may enable pathological delineation of nevi from melanomas. The device should yield a sensitivity/specificity of 99%/99%. As an intermediate between dermoscopy and biopsy, this technology will improve early melanoma detection by surveying more lesions while reducing unnecessary biopsies.

Dana Orange, MD: *Evaluating T Cell Specificity in Rheumatoid Arthritis.* The role of adaptive immunity in rheumatoid arthritis (RA) is still hotly debated. Some argue that T cell responses in RA are not antigen-specific but rather result from nonspecific proliferation in response to aberrant cytokines produced from the cells of the innate immune system such as macrophages and neutrophils, as well as synovial fibroblasts. There are several reasons to believe specific aberrant T cell responses may indeed be involved in disease pathogenesis. This project will evaluate whether patients with RA have expanded T cell populations specific to the same antigens to which they have antibody responses.

Ana Pereira, MD: *Glutamatergic Dysfunction in Cognitive Aging: Riluzole in Mild Cognitive Impairment and Normal Cognitive Aging.* Cognitive aging is a major source of disability and its prevalence will increase as the population ages. The paucity of effective treatments for cognitive aging disorders makes it important to focus on developing novel therapeutics. Riluzole, a glutamate modulator agent with a good safety profile in humans, will be tested in patients with mild cognitive disorder and normal cognitive aging patients with cognitive complaints. Cognitive functional changes, along with in vivo biomarkers such as MR spectroscopy and cerebral perfusion studies will be evaluated in these patient populations.

Jeremy Segal, MD, PhD: *Intrinsic and Extrinsic Aging-Related Changes In Epidermal Stem Cells and Their Impact on Skin Aging.* The project will have important implications not only for stem cell biology and aging in general, but will help shed light on some of the intricacies of tissue organization and its inherently complex cellular intercommunication.

Ana Tuyama, MD: G*ene and MmicroRNA Expression Profile of Hepatocytes and Hepatic Stellate Cells from Obese Patients in Defined Stages of Non-Alcoholic Fatty Liver Disease.* Non-Alcoholic Fatty Liver Disease (NAFLD) is the most common cause of chronic liver disease (CLD) in the Western World, affecting approximately 34% of the US population. The rates of NAFLD are rising and parallel the alarming epidemics of diabetes and obesity. This project will study the gene and microRNA (miRNA) expression pattern of hepatocytes and hepatic stellate cells in histologically and clinically defined stages of NAFLD in morbidly obese patients undergoing bariatric surgery. A more detailed analysis at the molecular level will help identify genes and highlight pathways that contribute to disease progression.

Upcoming Seminars in Clinical Research

November 30, 2011	Dr. Maria Pascual, Baylor Institute for Immunology Research
December 7, 2011	Dr. Monica Sweeney, Deputy Commissioner of Public Health
December 14, 2011	Dr. Stephen Nimer, Memorial Sloan-Kettering Cancer Center
January 4, 2012	Dr. Timonthy Wang, Columbia University College of Physicians and Surgeons

For future seminar schedules, please go to http://www.rucares.org/.

Discoveries Advancing Medicine: Why is it so hard hard to lose weight?

By Elizabeth (Betsy) Hanson

In the late 1950s, when Jules Hirsch became interested in studying obesity, most scientists considered fat, or adipose tissue, to be inert—a passive insulator in which the body stores energy in the form of triglycerides. Over the next decade, in the first studies on human fat metabolism, Hirsch gained fundamental insights into the normal function of fat in the human body and how this differs in the obese.

This groundbreaking research depended on long-term observations of patients in the Rockefeller Hospital, the proximity of state-of-the-art chemistry laboratories, and the ability to carry on research between these two arenas. Hirsch had worked for several years with Edward H. Ahrens, Jr. (1915-2000) at Rockefeller, perfecting techniques for separating fats, or lipids, from other compounds and from each other. It was the heyday of technology for chemical separation—in other Rockefeller laboratories a method called countercurrent distribution was being developed, and chemists were inventing tools to analyze amino acids.

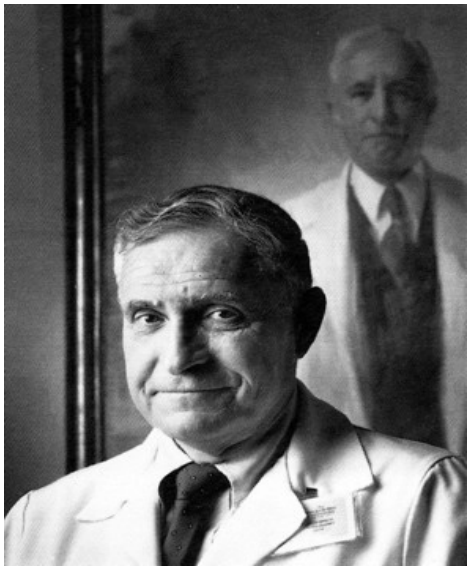
Hirsch first developed a method of silicic acid chromatography for separating complex lipid mixtures. He also experimented with columns using factice, and demonstrated the use of differential refractometry for precisely monitoring column eluates—a method later incorporated into high performance liquid chromatography.

These powerful tools helped launch Hirsch on investigations into obesity that he has pursued for decades. Little research had been done on human adipose tissue because the large samples needed were difficult to obtain. But the new separation techniques made it possible to analyze lipids in very small samples, and Hirsh devised a simple way to obtain these from human subjects by drawing the tissue out in a syringe.

In studies at the Rockefeller Hospital, Hirsch fed patients precisely defined formula diets and discovered that the composition of fat in adipose tissue mirrored the fat in the diet for both obese and lean individuals. In addition, the tissue was metabolically active, taking up glucose and fat, and releasing fat at rates readily changed by hormones such as insulin and epinephrine.

During these first studies of obese individuals, Hirsch also discovered that restricted calorie diets had effects beyond weight loss—his patients showed physiological signs of semi-starvation, such as slower heart rates, feeling cold, and lowered white blood cell counts. They also became depressed and preoccupied with food, and they developed a distorted body image, seeing themselves in the mirror as heavier than they actually were. Hirsch's behavioral observations of human subjects provided further evidence that adipose tissue had an important regulatory function in the body, and they pointed the way to a new phase of research, the study of fat cells.

Jules Hirsch received his undergraduate education at Rutgers University and earned the MD at Southwestern Medical School, University of Texas - Dallas (1948). After an internship at Duke University Hospital and residencies at Upstate Medical Center in Syracuse, NY, he joined the Rockefeller Institute in 1954. Hirsch served as Physician-in-Chief of the Rockefeller University Hospital from 1992 to 1996, and chairman of the institutional review board from 1984 to 1996. He has been president of the Association for Patient-Oriented Research and the American Society for Clinical Nutrition, and contributed as an editor or editorial board member to more than a dozen journals. Among many honors and awards, Hirsch has been elected to the Institute of Medicine, and he received the Stunkard Lifetime Achievement Award from The Obesity Society in 2006.



Dr. Jules Hirsch