Center News

Center for Clinical and Translational Science Awarded $22 million, 5 Year CTSA Renewal Grant

By Editorial Staff

The Rockefeller University Center for Clinical and Translational Science (CCTS) was awarded $22 million to support 5 additional years of research under the Clinical and Translational Science Award (CTSA) program funded by the NIH National Center for Advancing Translational Science (NCATS). Drs. Barry Coller and James Krueger serve as Co-Principal Investigators of the new award and Maija Williams, MPH serves as and Administrative Director. The CTSA also supports the Rockefeller KL2 Clinical Scholars Program, which is a 3-year Master's degree program for doctoral level health professionals. Dr. Sarah Schlesinger serves as the Director, in the Rockefeller University Hospital, with the University providing the balance of the funding. This includes experts in bioinformatics, biostatistics, research nursing, research pharmacy, clinical research coordination, research participant recruitment, protocol development, protocol monitoring and auditing, bioinformatics, information technology, regulatory compliance, and protection of human participants. The Rockefeller University Advisory Committee for Clinical and Translational Science (ACCTS) is the governing body of the CCTS and reviews all protocols for scientific integrity, participant safety, and resource utilization before they are

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Hospital Hallway Project to Honor 11 Outstanding Women Scientists at Rockefeller

By Editorial Staff

Stimulated by a suggestion by the campus organization Women in Science at Rockefeller (WISER), and Dr. Leslie Vosshall, head of the Laboratory of Neurogenetics and Behavior, the Hospital leadership embarked on a project with Olga Nilova, Special Collections and Operations Librarian in the Markus Library, Kate Kadoun, Senior Director, Volunteer Support and Donor Relations, and Jennifer Ashlock, Development Communications Specialist, to update the Hospital's first floor hallway display with placards depicting 11 outstanding women scientists at Rockefeller. The list includes:

• Alma E. Hiller, PhD – The Discovery of Hydroxylysine and the Birth of Clinical Chemistry
• Marie Maynard Daly, PhD – The Chemistry of Histones
• Clara J. Lynch, PhD – Deciphering the Genetics of Cancer
• Clara Nigg, PhD – Cultivating and Characterizing Rickettsia Prowazekii
• Florence Sabin, MD – Embryology of Hematopoiesis and the Role of Monocytes in Tuberculosis

• Lillian E. Baker, PhD – The Birth of Tissue Cultures of Human Cells
• Louise Pierce, MD – Discovery and Successful Clinical Trials of Tryparsamide
• Margaret Pittman, PhD – Characterization and Development of Serotherapy of Hemophilus Influenzae
• Nancy P. Ellicott, RN – The Birth of Research Nursing
• Rebecca C. Lancefield, PhD – The Chemistry and Classification of Streptococci
• Mary Jeanne Kreek, MD – The Development of Methadone Maintenance Therapy and the Biology of Addictive Disease

In addition, a series of historical photos of the hospital are displayed, including scenes of the construction of the hospital and its annex, an early ambulance, the World War I demonstration hospital erected adjacent to the Hospital for training personnel to treat injured soldiers in France, the first oxygen chamber to treat patients with pneumonia, the laboratory of Dr. Oswald Avery, and a typical early ward in the Hospital.

Dr. Barry Coller, Physician-in-Chief of the Hospital, commented, “By highlighting the groundbreaking and landmark research of these 11 outstanding scientists, the display is designed to serve as an inspiration for all members of the Rockefeller community.”

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reviewed by the Rockefeller University Institutional Review Board (IRB). Dr. Robert Darnell serves as ACCTS Chair, and Dr. Dana Orange, a graduate of the Clinical Scholars Program, serves as Vice-Chair.

The grant proposal included four specific aims, which are listed below.

1. To provide a robust infrastructure to conduct clinical investigation at the highest levels of participant safety, scientific rigor, bioethics, and regulatory compliance.
2. To ensure that every discovery at Rockefeller has its best chance of improving human health.
3. To educate the entire research workforce in conducting translational research at the highest level of participant safety, scientific rigor, bioethics, and regulatory compliance.
4. To study and improve the clinical research enterprise both at Rockefeller and nationally.

Dr. Schlesinger commented, “We are enormously proud of the accomplishments of the Clinical Scholars and role they play in supporting clinical and translational science in both basic and clinical laboratories on campus. The more than 60 graduates of our program are leaders in clinical and translational science around the world, using the skills and experience they obtained in the program to improve human health globally.”

Dr. Krueger noted, “We are delighted that NCATS judged our proposal worthy of an additional 5 years of support since the infrastructure we have built as a team to support both our scientific and educational programs, including the Clinical Scholars Program and the Certificate in Clinical and Translational Science Program, is outstanding and plays a vital role in ensuring that all of our research is conducted to the highest levels of scientific quality and participant safety. Dr. Coller added, “We take great pride in knowing that many of the innovative programs we have developed at Rockefeller under the CTSA program are now being adopted at sites across the CTSA consortium, including our Research Navigation program under Donna Brassil, our Research Participant Perception Survey under Dr. Rhonda Kost, our Clinical Research Nursing

initiatives under Dr. Candy Capili and Rita Devine, RN, MPA, our community-engaged programs linked to basic mechanistic science under Dr. Jonathan Tobin and Dr. Kost, our bionutrition program under Andrea Ronning, MA, RD, the role of the Research Hospitalist under Dr. Barbara O’Sullivan, our Biostatistics educational approach under Dr. Roger Vaughan, and our Bioinformatics program, which supports software development, data analysis, data sharing, and systems support under Dr. Yupu Liang and Prasanth Manukonda, MA, MS. We are extremely excited about the new initiatives included in our new grant proposal and look forward to a stimulating and productive next 5-year grant period.”

Center for Clinical and Translational Science Awarded $22 million, 5 Year CTSA Renewal Grant

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Remembering Dr. Mary Jeanne Kreek: The Total Package

By Rita Devine, MPA, RN

The news of Dr. Mary Jeanne Kreek’s passing was felt by many in the Rockefeller University community, and the Hospital personnel felt it keenly. Dr. Kreek worked closely with the nursing staff and the Pharmacy Department to conduct her research and provide treatment, which had a large impact on countless lives from the participants to caregivers to physicians. Her work not only yielded new treatments for these disorders, but also influenced societal attitudes toward them. Physician-scientist Mary Jeanne Kreek, the Patrick E. and Beatrice M. Haggerty Professor and a senior attending physician at The Rockefeller University, was best known for her research into the biology of drug and alcohol addiction.

I think everyone recalls their first meeting with Dr. Mary Jeanne Kreek – I clearly remember mine. As the new Clinical Operations Manager, I was invited/summoned on September 7, 2010 to the weekly Tuesday Laboratory of the Biology of Addictive Diseases meeting in Hospital Room 128. I was intimidated – her reputation was legendary; “intense, no nonsense, she will size you up in a minute” was what I was told to help prepare me for my meeting. I intended to sit and observe, but Dr. Kreek had “saved” the seat directly across from her and the questioning began. Everything I heard about her was true, she was fierce and passionate about her research and did not have time to handhold anyone connected with her research.

I quickly realized I was in the presence of a truly brilliant and amazing woman. From that day forward, I attended almost every lab meeting. Her knowledge and expertise were outstanding, and one learned so much observing her in action. I asked if I could bring one of the staff nurses, as I felt it was important for members of the nursing staff be exposed to great research. Attending the Kreek lab meeting became part of the clinical research nursing orientation. All nurse attendees were awestruck by Dr. Kreek’s level of knowledge and her passion to

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2021 Heilbrunn Nurse Scholar Recipients

The Heilbrunn Nurse Scholar awards are now in the eighth year of supporting nurse-led research projects. Since 2014, twenty-eight nurse scientists have received this award. This April, five additional Heilbrunn Nurse Scholars were selected. The award is highly competitive and reviewed by a committee of senior scientists from around the country; it is administered by the Heilbrunn Family Center for Research Nursing. Each award provides a maximum of $25,000 for one or two years. Funding for the awards is from an endowment established by Helaine Lerner and Joan Rechnitz in honor of their parents, Harriet and Robert Heilbrunn. For the 2021 award cycle, applications were submitted by doctoral nursing students and postdoctoral nurses across the United States from 19 institutions.

The recipients of the 2021 cycle will study a variety of topics ranging from characterizing vulvodynia in women with hypermobility spectrum disorders to the longitudinal investigation of inflammatory marker profiles in overweight and obese women with and with preeclampsia.

The 2021 Recipients:
Ms. Jen Glayzer is a 4th-year full-time student in the Bachelor of Nursing Science to Doctor of Philosophy in Nursing at the University of Illinois Chicago. She will characterize vulvodynia and Ehlers-Danlos syndromes (EDS)/hypermobility spectrum disorders (HSD) pain and determine pain phenotypes. EDS and HSD are hereditary soft connective tissue disorders that affect an estimated 1 in 5,000 people, with 90% having devastating chronic pain. There is little research characterizing EDS/HSD pain and no study describing vulvodynia in EDS/HSD. She will examine generalized pain and vulvar pain in a cross-sectional convenience sample using an online survey accessed via links in EDS/HSD and vulvodynia support groups on Facebook and Reddit.
Cassandra Godzik, PhD, RN, is a practicing psychiatric mental health nurse practitioner and postdoctoral research fellow in the Departments of Psychiatry and Community and Family Medicine at Dartmouth-Hitchcock Medical Center (DHMC), Centers for Aging at Dartmouth, and Geisel School of Medicine at Dartmouth. She will study insomnia in older adults by analyzing their home sleep environments using a novel technology, the Phillips SmartSleep, and Self-Report. Study participants will be recruited from primary care clinics from Northern New England.
Sara Mithani, PhD, RN is a postdoctoral fellow at the National Institutes of Health/National Institute of Nursing Research. She will utilize the clinical data and stored blood samples from the largest multi-center longitudinal study of current and former U.S. military persons and Veterans with combat exposure. Her research aims to examine the relationship of exosomal cargo and activity in a sample of Veterans who sustained mild traumatic brain injuries (TBI) and link the exosome levels to chronic neurological symptoms and neurologic deficits.
Seydahtanaz Saidzadeh, PhD, RN is a postdoctoral fellow at the University

Dr. Connie Ulrich Delivers the 2021 Beatrice Renfield Lectureship in Research Nursing

By Bernadette ‘Candy’ Capili PhD, NP-C

The Rockefeller University Center for Clinical and Translational Science (CCTS) and the Heilbrunn Family Center for Research Nursing hosted the 13th Annual Beatrice Renfield Lecture in Research Nursing on March 23, 2021. The lecture was held virtually this year due to COVID-19 restrictions. Dr. Barry Coller, Physician-in-Chief of the Rockefeller University Hospital, began the event with a short tribute to Ms. Nancy Ellicot, Rockefeller University Hospital's first Superintendent of Nursing, who established the standards for the practice of clinical research nursing and invented several novel devices to improve nursing care.

Dr. Bernadette ‘Candy’ Capili, Director of the Heilbrunn Family Center for Research Nursing, hosted the program and introduced this year’s speaker, Connie Ulrich, PhD, RN, FAAN. Dr. Ulrich is the Lillian S. Brunner Chair in Medical and Surgical Nursing and a Professor of Bioethics and Nursing at the University of Pennsylvania School of Nursing, with a secondary appointment in the Perelman School of Medicine, Department of Medical Ethics and Health Policy.

Dr. Ulrich’s presentation, “Ethics: Emerging Issues and Trends in Clinical Research,” focused on her original research on recruiting and retaining research participants. She also addressed the perceived value of informed consent, digital technologies in research, and social media for recruitment in clinical research. Dr. Ulrich is an internationally recognized expert in empirical research bioethics. Her work has been funded by the NIH and other federal and state agencies.

In her presentation, Dr. Ulrich discussed reasons participants join or do not join research studies. She presented the top benefits and concerns identified by participants when joining a study. The presentation concluded with an important take-home message for the research community in how important the study team is to the participant experience. She emphasized how the style of communication with the study team can enhance retention of participants in research studies.

One hundred and ninety-three guests attended the lecture, including representatives from the Heilbrunn Family, the Beatrice Renfield Foundation, members of the Rockefeller University Hospital Nursing Department, and the CCTS Clinical Research Support Office, Facilitation Office, Regulatory Affairs Group, and Bio-Statistics Group, as well as members of Rockefeller Laboratories. Also in attendance were six Heilbrunn Nurse Scholars. Dr. Ulrich’s presentation was webcast by the Clinical Director’s Network (CDN).
Clinical and Translational Science (CCTS) and the Yale Center for Clinical Investigation (YCCI) participated on a Zoom meeting, continuing the tradition of annual Collaborative Research Day meetings between Yale and Rockefeller that began in 2008. This year's event, like those in the past, provided a great opportunity for trainees and junior faculty from both institutions to discuss their current research studies, develop collaborations, and discuss topics of mutual interest. Dr. Sarah Schlesinger, Program Director of Rockefeller University Clinical Scholars program and Dr. Brian Smith, Co-Director of YCCI warmly welcomed the attendees.

The first event of the day was the Clinical Scholars' talks presented by Dr. Rachel Niec from Rockefeller, and Dr. Elizabeth Goldfarb from Yale. Dr. Niec's presentation, *Lymphatic Capillaries Regulate the Intestinal Stem Cell Niche*, focused on understanding how vasculature regulates the integrity of barrier surfaces, including in the intestinal tract and skin; specifically, how lymphatics interact with stem cells to promote their function in health and disease. Dr. Goldfarb's presentation, *Implications of Stress-Related Memory Biases for Fear and Drinking*, explored how stress-related memory biases can impact fear responses and drinking behavior in the real world.

The afternoon was dedicated to 10-minute pin-point oral presentations and a panel discussion from Yale and Rockefeller Clinical Scholars. The nine presenters all gave sophisticated, high-level talks on their respective research projects. From Rockefeller, Dr. Dana Bielopolski presented *Obesity-Related Glomerulopathy in Adolescents, A Big Data Study*, describing her big data analysis of the effect race and body mass index (BMI) on estimation of kidney function. She concluded that in the era of tailored medicine, nephrology should aspire to reduce standardization and embrace a more individualized approach to patient assessment.

Dr. Mira Patel spoke on *Germline ApoE as a Predictive Biomarker in Cancer*, and discussed the role of immunosurveillance in mechanisms of cancer progression and metastasis, particularly as it relates to germline genetic variants that may predispose to metastatic disease. Dr. Yael Renert-Yuval's talk, *The Molecular Features of Normal and Atopic Dermatitis Skin in Infants, Children, Adolescents, and Adults*, comprehensively explored the transcriptomic dysregulation in atopic dermatitis skin across various pediatric age-groups as compared to adults as a way to improve our understanding of the disease mechanism and identify novel treatment targets.

Dr. Rashid Rumah presented *Could Multiple Sclerosis be Triggered by A Bacterial Neurotoxin*, in which he examined the clinical evidence supporting *Clostridium perfringens* epsilon toxin as a possible triggering factor for multiple sclerosis.

From Yale, Dr. Juan Vasquez spoke on *Alterations in the Immune Landscape of Childhood Leukemia*. Dr. Vasquez described the use of combined mass cytometry and single cell genomics showing evidence of immune exhaustion and identifying distinct immune phenotype-based clusters correlating with disease risk in acute lymphoblastic leukemia. Dr. Elise Liu’s talk on *The Role of Peanut-Specific IgA in Peanut Allergy* reviewed the role of peanut-specific, food-specific immunoglobulin A as a central step in the immune response to food antigens.

Dr. Alicia Little spoke on *The Role of HIF1a in Chronic Cutaneous Lupus Erythematosus*, and described the role of HIF1 in chronic cutaneous lupus erythematosus in a mouse model and human skin samples. Dr. Gunjan Tiyyagura presented *Development and Validation of a Natural Language Processing Algorithm to Identify High-Risk Injuries in Infants Concerning for Physical Abuse*. The investigators developed and described the accuracy of a natural language processing algorithm that identified high-risk injuries associated with abuse in infants.

Dr. Kathleen O’Neil’s presentation, *The Effect of the COVID-19 Pandemic on Community Violence: Minority Communities*. In this study of community violence in Connecticut during the continued on Page 8
CTSA Research Pharmacies and Rapid Phase 1 Trial Startup During the COVID-19 Pandemic
By Robert B. MacArthur PharmD, MS, BCSCP

The term “Translational Pharmaceutics” refers to the development of drug formulations in parallel with performing Phase 1 studies to develop promising drug products safely, efficiently, and rapidly. The Rockefeller University Hospital (RUH) participated in a translational pharmaceutics COVID-19 research project that was included in a survey performed by the Clinical and Translational Science Awards (CTSA) program. The full CTSA survey results were recently published in the Journal of Clinical and Translational Science as ‘Re-engineering The Clinical Research Enterprise in Response to COVID-19: The Clinical Translational Science Award (CTSA) Experience and Proposed Playbook for Future Pandemics’. The RUH project is described in the companion paper, ‘CTSA Pharmacies: Contribution to Research and Public Health during the COVID-19 pandemic’. The pharmacy survey and results were developed and interpreted by the CTSA Pharmacy Discussion Forum, a collaborative team of pharmacists and physician-investigators from The Rockefeller University Hospital, Albert Einstein College of Medicine, The Mayo Clinic, The University of Pennsylvania, and Duke University Hospital.

A key overall finding from the survey was the importance of research pharmacy services across CTSA institutions nationwide, as most academic medical centers (AMCs; 84%) relied on their research pharmacies to support COVID-19 research initiatives. Many AMCs expanded research pharmacy hours and staffing to support the rush of COVID-19 research.

Regarding the translational pharmaceutics project performed at RUH, the project began in late March 2020, by bringing together the toxicology, formulation, and human safety data required for a Investigational New Drug Application (IND). Most of the data were generated under a previously filed IND for an inhaled hydroxychloroquine (HCQ) product intended for the treatment of asthma. One objective of the RUH project was to repurpose the product for treatment of COVID-19 pneumonia, relying on the recognized immunomodulatory and potential antiviral effects of HCQ. Since HCQ was in short supply, the RUH pharmacy had to search the globe for a supplier of HCQ, the active pharmaceutical ingredient. It then had to perform all of the formulation development work, and contract with formulation testing laboratories to ensure the integrity of the drug product. Sterile compounding was performed by the RUH hospital pharmacy working closely with the physician investigators (Figure 1).

Thus the formulation of a sterile HCQ solution suitable for both inhalation and delivery by a commercially available nebulizer was developed during the month of April 2020, and solution vials were placed into initial stability testing by early May 2020. In parallel, the Principal Investigator, Chief Clinical Scholar Dr. Ohad Bentur, and the study team compiled the necessary toxicology, chemistry, and human safety data. A figure depicting the different IND components that were organized and submitted is provided in Figure 2.

The IND application was filed with the FDA under an Emergency Use Authorization (EUA), in mid-May. The EUA allowed the Food and Drug Administration (FDA) to work closely with the investigators, regulatory experts, and formulators, and IND-related correspondence was exchanged with the FDA once or twice weekly. With that level of attention and close communication between the FDA and study investigators, the FDA allowed the study to proceed by early June. The Rockefeller IRB approved the Phase 1 trial protocol by mid-June, and the first subjects were enrolled during the last week of June. Thus, the time from project inception to first subject dosing was an amazingly short approximately three months. Dr. Bentur presented the results of the study, which demonstrated that the inhaled HCQ was well tolerated by healthy volunteers, at the meeting of the American Academy of Allergy, Asthma & Immunology in late February 2021.

Drug development programs, especially those testing complex drug: device formulations are now commonly incorporating translational pharmaceutics approaches. The RUH Phase 1 protocol described demonstrated how CTSA institutions can apply innovative research methods to address critical clinical research initiatives and speed the development of protocols involving experimental drugs.
NCATS Highlights Research by Clinical Scholar Tobias Becher and Head of Laboratory Paul Cohen on Brown Fat

By Editorial Staff

Under the title, CTSA Program-Supported Researchers May Turn Brown Fat into an Ally Against Obesity, the NIH National Center for Advancing Translational Sciences reported on its web site studies published in Nature Medicine by Clinical Scholar graduate Dr. Tobias Becher and his mentor Dr. Paul Cohen, head of the Laboratory of Molecular Metabolism. The article focused on how they applied ‘translational science approaches to expand the understanding of brown fat in humans as a potential therapeutic target for blunting obesity’s deadly impact on people’s cardiovascular and metabolic health.’ Figure 1 reprinted from the article, which stressed the potentially protective effects of brown fat, which burns energy to produce heat, as compared with white fat, which stores excess energy and results in disturbed lipid and carbohydrate metabolism.

Babies are born with a relatively large amount of brown fat, but then begin to lose it with age, such that older adults usually have no or very little brown fat. They took advantage of the ability to detect brown fat in positron-emission tomography (PET) scans, commonly used to detect malignancies to categorize people based on presence and absence of brown fat. By forging a collaboration with colleagues at Memorial Sloan Kettering Cancer Center, they were able to analyze data from more than 130,000 PET scans from more than 52,000 patients. They found that cardiovascular and metabolic disorders were less frequent in patients with brown fat, with significant reductions in the prevalence of type 2 diabetes, high cholesterol and triglycerides levels, coronary artery disease, and high blood pressure. Brown fat even offered protection among obese patients, and its effects seemed to be most pronounced in this subcohort.

These studies required advanced statistical analyses performed in collaboration with Dr. Roger Vaughan, Director of Biostatistics in the Center for Clinical and Translational Science at Rockefeller, and Caroline Jiang, MS, Senior Biostatistician. Dr. Cohen emphasized this aspect of the research by noting that Tobias’s translational training in the Clinical Scholars program, “allowed Tobias to employ high-level biostatistics and to collaborate with very experienced biostatisticians at the Rockefeller CTSA to analyze the data. Without those kinds of links and collaboration, this research work would never have come together.” The next steps in this research will involve assessing the relative contributions of environment, genetics, and aging on preserving brown fat. Exposure to cold and aerobic exercise are known to increase brown fat, and so may also be important to consider in future research.

Remembering Dr. Mary Jeanne Kreek: The Total Package

continue to learn and teach always with an eye to the future to meet unmet needs in the addiction community. Dr. Kreek was a genuine advocate for Rockefeller nurses. Her memory was astonishing, and she often spoke of former participants and their positive interactions with the nursing staff. She appreciated us, she supported us, she respected us, and the feelings were truly mutual.

Over the years, I was invited to “stay for a minute” after lab meetings, often while she finished her lunch. As Nursing Directors moved on, she encouraged me to apply for the position of Director of Nursing and Patient Care Services. I felt her pride when I told her I was accepted for the position and how much I appreciated her advice. I was so fortunate to experience the other side of Dr. Mary Jeanne Kreek—the wife, the mother, the grandmother, the advisor, and the friend. She really was the total package, and we will miss her.
of Wisconsin-Madison. Saidzadeh's study will develop a psychoeducational intervention for anxiety and depression for post-treatment head and neck cancer (HNC) survivors. HNC survivors encounter many mental challenges during and after treatments, including anxiety, depression, persistent debilitating physical symptoms (e.g., difficulty swallowing), and facial disfigurement, which can be emotionally overwhelming.

McKenzie Wallace, PhD, RN is a postdoctoral fellow at the University of Pittsburgh. Dr. Wallace will examine the inflammation pathway among overweight and obese pregnant women as it relates to adverse pregnancy outcomes, specifically preeclampsia (PE). Obese women are much more likely to develop PE; however, the mechanism for why some overweight/obese women develop PE while others do not is not well understood. PE is one of the leading causes of maternal and infant morbidity and mortality. To address this gap, Dr. Wallace will explore 20 inflammatory markers and IL6 and IL10 genetic variants in an existing sample of 129 overweight and obese women with and without PE to further investigate the relationship between inflammatory marker profiles and PE.
COVID-19 public health crisis, we found that violence-related trauma significantly increased overall, but particularly in Black/Latino communities as compared to the white population.

The unmet clinical need brought upon by the SARS-CoV-2 pandemic required a multi-disciplinary response. Four scholars, each conducting very different types of research on the same disease, presented their work on COVID-19 related projects in a special panel discussion. The COVID-19 pandemic caused a shift in many scientists’ research focus and the panel discussion highlighted those changes. The Rockefeller panelists were Dr. Ohad Bentur, who presented Development of Aerosolized Hydroxychloroquine Sulfate for Respiratory Tissue-targeted Treatment of COVID-19, Dr. Christian Gaebler, who discussed Evaluation of the Anti-SARS-CoV-2 Humoral Immune Response in a Cohort of COVID-19 Convalescent Individuals. The Yale panelists, Dr. Tara Alpert, who spoke on Early Introductions and Community Transmission of SARS-CoV-2 Variant B.1.1.7 in the United States. The SARS-CoV-2 variant B.1.1.7 was introduced to the United States in early December 2020 and soon became established within many communities. The primary points of entry into the US are identified as NY, CA, and FL, and exponential growth in these states resulted in spread to neighboring states. Ms. Jillian Armstrong, SARS-CoV-2 in Connecticut Nursing Homes: Vaccine Effectiveness and Repeat Positive Testing. Ms. Armstrong presented a retrospective cohort analysis of two Connecticut skilled nursing facilities found partial vaccination with Pfizer-BioNTech COVID-19 vaccine (from >14 days after dose 1 through 7 days after dose 2) to be 63% (95% confidence interval = 33%–79%) effective against SARS-CoV-2 infection and our retrospective analysis of state-wide Connecticut nursing home residents during the initial 9 months of the pandemic found that 2.6% of residents had a repeat positive SARS-CoV-2 test result 90+ days after their initial infection. The research conducted by these four Scholars spanned from basic science to clinical interventional studies and to epidemiological studies. Dr. Bentur presented results of a Phase I study with aerosolized hydroxychloroquine that was conducted in the Rockefeller University Hospital. He highlighted the importance of the skills he acquired in the Clinical Scholars Training Program enabled him to conduct this study. In less than three months, he submitted an Investigational New Drug (IND) application to the FDA, gained IRB approval for the protocol, and enrolled the first participant. In April 2020, during the peak of the COVID-19 pandemic in New York City, Dr. Gaebler and his team enrolled more than 150 participants who had recovered from COVID-19 and began studying their antibody responses. This led to the identification of B lymphocyte cells making broadly neutralizing antibodies to SARS-CoV-2, and the genes for these antibodies were cloned, leading to the selection of a combination of two of the antibodies as a treatment for COVID-19. These antibodies are now being tested in human studies.

When asked for feedback on the day, Dr. Renert-Yuval commented, “Despite the known deficiencies of virtual meetings, the small groups workshops gave an opportunity to present research in a supportive and friendly atmosphere. It provided a glimpse into interesting projects conducted at both sites, some of which were surprisingly complementary.” Dr. Bielopolski noted that, “It was a great environment and atmosphere in which to present my work orally for the first time, and I am glad I had the opportunity to meet and hear other translational colleagues. I wish all of us that next year’s meeting will be in person.” Dr. Niec also provided her thoughts, “It was a wonderful opportunity to share and hear interesting research with our Yale colleagues. The small setting provides a great chance to develop collaborations.”

Dr. Barry Coller, Co-Director of the Clinical Scholars Program and CCTS and Dr. Smith closed the event by thanking everyone for creating another very successful collaborative event. Rockefeller will host the next Research Collaboration Day in 2022, and we look forward to the event being once again, in-person.
Meet the Graduate: Anita Shet, MD, PhD

By Editorial Staff

Dr. Anita Shet joined the Clinical Scholars Program at the Rockefeller University in 2003 in the laboratory of Dr. Martin (Marty) Markowitz at the Aaron Diamond AIDS Research Center. Dr. Shet received her MBBS from Bangalore University, MD from the University of Minnesota School of Medicine, and PhD from Karolinska Institute.

Dr. Shet is a pediatric infectious diseases specialist with broad interests in childhood infections in low and middle-income countries, including pediatric HIV and vaccine-preventable infections. She is the Director of Child Health, International Vaccine Access Center, and Senior Scientist in the Department of International Health at Johns Hopkins Bloomberg School of Public Health. She leads a multicenter study on clinical pneumonia in children and is evaluating the impact of the pneumococcal conjugate vaccine rollout in India. Her research also explores the link between timely immunization and cognitive outcomes in children. Dr. Shet has recently been appointed as Director of Johns Hopkins Maternal and Child Health Center in India that focuses on enhancing women’s health, saving newborn lives, addressing vaccine-preventable diseases, and strengthening public health capacity in India.

How did you get interested in research? Were you always interested?

Seeking the reasons for why things were the way they were, had always piqued my interests from childhood. My family would call me the ‘why-why girl’ when I was young, often with a tinge of exasperation as I was apparently never satisfied with their usual answers. During medical school in India, my involvement with research projects gave me a sense of how deep one has to dive into the subject to get answers. Of course, there was never enough time – life took me through residency and fellowship in the US, and I became immersed in clinical medicine. My mentor at the University of Minnesota, Dr Edward Kaplan gave me the opportunity to get my hands wet with laboratory work, and I found this fascinating. And then when chance brought me to Rockefeller University when I followed my husband Arun Shet who joined the Clinical Scholar’s program, and I learned about Barry Coller and his achievements, and saw the opportunity to work with Marty Markowitz and David Ho at the Aaron Diamond AIDs Research Center, I was captivated.

How did you come to Markowitz Laboratory?

As I was finishing up my fellowship at the University of Minnesota in 2003, India was going through a difficult time with HIV. The previous decade was spent in denial that HIV existed in India, and then when the evidence spilled over, the stigma was so great that it was the rare health worker who elected to work in this area. And ‘cocktail therapy’ – the use of multiple drugs with different mechanisms of action at the same time, a paradigm-shifting discovery by David Ho at Rockefeller University, was becoming standard of care in the US. I wanted to learn more about how the drugs worked in people, and how patients responded to medical care both physically and mentally, so I was a privilege to work as a physician at the Rockefeller Hospital and also do research at the same time. Marty and I would have clinic starting at 7 am at Rockefeller, where I enjoyed providing medical care, but mostly listening to the evocative stories of patients and their thoughtful questions, and then we would take blood samples ourselves and carry them over to the lab by afternoon to do our experiments. It was a fulfilling time of learning at every step – everyone was my teacher, apart from Marty and Barry – the patients, the nurses in the clinic, the lab technicians, and my wonderful Clinical Scholar colleagues, each an expert in his or her own way.

What is your current research?

My research journey took quite the scenic route. The physician-scientist skills I picked up at Rockefeller held me in good stead as I dabbled in translational research in India and established a clinical cohort of HIV-infected children who we were able to follow long-term. During the decade I spent in India on the frontlines of medical care for children, I became increasingly aware of the limitations of what a physician sitting in a clinic can do. This drove me to explore public health, and I pursued a doctorate in Public Health Sciences at Karolinska Institute in Sweden, and completed my thesis work in India. I decided to go into full-time research and teaching, which would allow me to work in primary preventative health and childhood vaccines. My current appointment is at the International Vaccine Access Center at the Johns Hopkins Bloomberg School of Public Health; and my projects include addressing vaccine-preventable childhood pneumonia, and socio-economic impact of vaccines, and more recently, understanding the impact of the COVID-19 pandemic on routine childhood vaccination in India and globally. At present I am the director of the maternal and child health center in India where we focus on capacity strengthening and public health research to enhance women and children’s health in India. We launched an open-access online course on "COVID-19 response in India: The impact on women and children's health and wellbeing"; and initiated several research projects with partner institutions on topics of implementation science in maternal nutrition, neonatal sepsis, SARS-CoV-2 immune response among healthcare workers, and COVID-19 vaccine acceptance among community health workers.

What were your expectations when you joined the Clinical Scholars Program?
program?

My expectations were exceeded by the Clinical Scholars program. I could not absorb enough – as there were so many interesting things to learn. One of my favorite parts was the tutorials with the Clinical Scholars that Barry organized, each time there was an intriguing topic that was discussed, often with interesting and illustrious guest speakers that Barry would invite to spend time with the Clinical Scholars, where we debated important topics. In the lab, I finally learned to hold the pipette correctly, and mainly to design and conduct my own experiments.

I was restless however – about the HIV situation in India. Daily I was learning about how women and children were bearing the brunt of this disease, and how they were being neglected; women at that time were given only a single drug as treatment, and children born and living with HIV were untreated as there were no formulations and they were expected not to survive anyway. So after three years of being a Clinical Scholar at Rockefeller, our family packed our bags and moved back to India.

What has been the most educational, interesting, and/or surprising aspect of being in the Clinical Scholars program?

When I look back, I feel every moment in the Clinical Scholars program was a learning opportunity.

Thinking back, one of my most poignant moments was listening to one of Marty’s HIV-positive patients who came back to the clinic after a long stint in the ICU, having recovered from a life-threatening infection caused by a virulent, highly-resistant Staphylococcus aureus infection, also called, ‘flesh-eating bacteria.’ I was struck by the images of his necrotic arm, which was, although healing, was severely disfigured by complete loss of muscle; but I was mostly intrigued by his story of how it all started with a skin boil, and how this was a common occurrence among other young people living with HIV. On the way to the lab, I discussed this with Marty, who casually suggested I study this if I want to know more. Startled, I indicated that his is a virology lab, so how can one study bacteria? One eyebrow raised, he looked askance as he said, ‘it’s up to you.’ That aphorism stayed with me throughout my career and life. Marty followed this up the same day by introducing me to his bacteriology colleagues, later helping me navigate the Rockefeller ethical review process to initiate a new human subject protocol and opening up his lab for me to study bacterial-viral interactions, and thus opened up a fresh chapter in my life.

Back home in India in 2003, I was able to establish a laboratory at the medical college where I joined as faculty, and set up HIV viral load testing and genotyping – techniques I learned with Marty. More than technical skills, it was the confidence I learned from my time as a Clinical Scholar that helped me with these activities. In the pediatric department I started an ‘infectious diseases clinic’ (a euphemism for HIV, as back then, one could not specifically name this infection) in order to bring infected children into care. We followed a similar pattern as we had done at the Rockefeller clinic; we would see children and families in the morning, and take their samples and conduct the tests in the afternoon, and counsel them with results soon after. My colleagues and I vigorously fought the existing meager national guidelines for single-dose one-drug therapy for pregnant HIV-positive women and obtained grants that would allow those in our hospital to receive the short-term 3-drug regimen, which brought down transmission rates of newborn HIV infection from 12% to 2%. We argued against the then-existing trend of not testing newborns at birth (guidelines said we should wait until 18 months to test them to know if they were infected or not, due to insensitivity of prevailing antibody testing techniques) and instead showed how we could use dried blood spot PCR testing to obtain results in the first few weeks of birth so that appropriate treatment could be instituted as early as possible. None of this would have been possible without the numerous teaching moments I encountered at Rockefeller University as a Clinical Scholar.

If you someone asked you to describe the Clinical Scholars program in one sentence, what would it be?

A program that takes one on a journey of self-realization, inspired by people who suffer from disease who happen to be one’s best teachers, instils the appetite for scientific discovery, and reveals the humility of knowledge.

Having graduated and in a new institution and position, what are the takeaways you would share with a junior Scholar?

Follow your heart, I would say, but know that you have the power to achieve your dreams. It really is up to you. As the Ranger asserted in JR Tolkien’s Lord of the Rings, ‘not all who wander are lost’. If you ever find yourself questioning, as I did, about what you are doing in the Clinical Scholar program, know that this will be one of your most significant career experiences, one that will carry lessons for life. Barry’s oft quoted vision of the ‘four-legged stool’ - of the continuum of the bench, the bedside and the community as the essence of translational medicine that brings about exceptional improvements in human health – is one that will influence you no matter where you travel in your career journey. As you look up to the giants constitute Rockefeller University, know that you will carry that legacy of inquisitiveness and spirit of discovery for humanity’s benefit, and one day become role models yourselves.
Meet the Scholar: Yael Renert-Yuval, MD

By Editorial Staff

Dr. Yael Renert-Yuval joined the Clinical Scholars program in July 2019 in the Laboratory for Investigative Dermatology mentored by Dr. James Krueger. She received her MD degree and completed her dermatology residency from the Hadassah-Hebrew University Medical School in Israel and spent a year as a research fellow at the Laboratory for Inflammatory Skin Diseases at the Mount Sinai Medical Center in New York. Dr. Renert-Yuval is a second year Clinical Scholar and will serve as Co-Chief Scholars in her third year starting July 2021.

How did you come to the Laboratory for Investigative Dermatology?

I was born and raised in Israel, which is where I went to medical school and completed my internship and residency in dermatology. During the 5-year residency program, there is a mandatory 6-month period that is dedicated to research, preferably basic science. My interest in research was strengthened during this period, that was extended to a year, in Dr. Emma Guttman's laboratory at Mount Sinai in New York. I had the opportunity to work on a range of exciting projects investigating inflammatory skin diseases. Some of these were in collaboration with the Krueger lab at the Rockefeller University. I loved visiting Rockefeller for joint meetings, and the research conducted in the Krueger laboratory was impressive, which encouraged me to apply to the Clinical Scholars program. The Clinical Scholars program was the ideal setting to allow me to continue working on projects that interest me, while at the same time to also expand my skills and knowledge. When I returned to Israel to finish my residency, I already knew that I wanted to come back to Rockefeller and the Krueger lab as a Clinical Scholar.

What is your current research?

My current research focuses on hidradenitis suppurativa (HS), which is a devastating skin disease in which patients suffer from painful, debilitating, and disfiguring lesions in flexural body regions, such as the axilla and groins. Affected patients have significant quality of life impairment because of the chronic pain, foul smells, and purulent secretions from involved areas. Unfortunately, although HS is not rare, therapeutic options are unsatisfactory and the disease is still poorly understood. We are taking psoriasis, a dermatologic disease where bench-to-bedside (and back) studies resulted in a highly efficacious and safe therapeutic repertoire, as a model for HS. By investigating HS and gaining better understanding of underlying mechanisms driving HS lesions, we want to understand the molecular abnormalities driving early HS and differentiating mild from severe disease. By doing that, we hope to identify biomarkers that will improve early HS diagnosis. Ideally, our results will also be able to guide therapeutic development by discovering novel therapeutic targets.

What were your expectations when you joined the Clinical Scholars program?

I was hoping to build a toolbox that will allow me to conduct a variety of clinical and basic science research projects by myself when I go back to Israel. Luckily, as a Clinical Scholar, I can conduct clinical trials and non-interventional patient-based studies encompassing a variety of inflammatory skin diseases. Across these studies, I take part in protocol conceptualization, writing, and approval, patient visits, scientific experiments, statistical analysis, and manuscript writing. I believe this experience and these new skills will be very useful in achieving my goal, which is to become a prolific clinical dermatologist and researcher.

What do you look forward to as Chief Scholar?

I always enjoyed sharing my experiences and helping colleagues in earlier stages of their programs, and I believe this is one of the most enjoyable aspects of my career in medicine/research. I cherish the opportunity to work with Drs. Schlesinger and Coller, who are truly inspirational to me as translational researchers and role models for supportive mentoring. I am also excited to work with my co-chief and friend, Rachel Niec, and I expect we will have a great experience being co-Chief Scholars.

What has been a learning opportunity or teaching moment as a Clinical Scholar?

When I started the program, I did not realize how important it is to communicate research to other people, with or without scientific background. As a clinician I am used to explaining diseases and treatments to patients but talking about science was completely new to me and surprisingly different, and it took me a long time to understand how to convey my message to others. One of the great aspects of talking about my research is that I have the learning opportunity to improve my skills, which still improves each time I talk about my research.

What has been the most educational, interesting, and/or surprising aspect of being in the Clinical Scholars program?

When I left the Guttman Laboratory almost 6 years ago, we started working on protocols in collaboration with the Krueger lab for clinical trials of biologic drugs for a common non-scarring inflammatory hair loss, called alopecia areata. When I started as a Clinical Scholar, one of the trials was already ongoing, and I was able to conduct patient visits at the Rockefeller hospital clinics, take part in data collection and analysis, data presentation to the funding sponsor, and manuscript writing. Although this was a relatively long study where patients were treated up to 72 weeks across two different medical centers, coming back as a Clinical Scholar provided me a unique opportunity to contribute to the entire process, from the initial concept to the completed paper, which is currently under review. We are now beginning research on transcriptomic analyzes of skin and blood samples collected during this trial.

If you someone asked you to describe the Clinical Scholars program in one sentence, what would it be?

A uniquely supportive environment allowing clinicians to build an array of research skills, personalized to their specific interests and needs.

What are your next steps/career goals when you graduate from the program?

In my final year in the Clinical Scholars program, I plan to join a pediatric dermatology clinic and become a pediatric dermatologist clinician-scientist when I go back to Israel. After my return to Israel, I plan to initiate new research projects focused on clinical unmet needs in pediatric patients. I also plan to continue working closely with the Krueger and Guttman Laboratories. Despite the challenges of the past year, it taught me that successful research collaborations can be conducted on virtual platforms.
Heroin abuse surged in the United States in the early 1960s, becoming a major public health problem. At the time, most people attributed addiction to a lack of willpower, or to antisocial or criminal behavior. The urgency of dealing with these issues came to the attention of Rockefeller researcher Vincent P. Dole (1913-2006) in 1962, when he was acting chairman of the Health Research Council of the City of New York’s committee on unresolved health problems, which was grappling with the heroin problem in New York. Dole proposed that addiction was an illness, a “metabolic” disease with behavioral manifestations. He was so committed to understanding this problem that he changed the focus of his laboratory, where he had studied obesity and metabolism, to heroin addiction and new pharmacological approaches for chronic treatment.

In late 1963 Dole recruited two additional researchers to the project: clinical investigator Mary Jeanne Kreek (1937-2021) and psychiatrist Marie Nyswander (1919-1986). In early 1964, this team began studies with heroin addicts at the Rockefeller Hospital which, within six months, established the mode of action and potential effectiveness for maintenance treatment of methadone, a synthetic drug that had been used for short-term detoxification in a few clinics. The researchers also contrasted methadone’s effects to the action of short-acting opiates such as heroin and morphine.

These early studies determined that methadone is long-acting in humans, relieves the addicts’ craving for heroin, and prevents withdrawal symptoms. In addition, methadone itself does not produce euphoria, and through the mechanism of cross-tolerance, it prevents addicts from feeling any “high” from an injection of heroin—a phenomenon the team called “narcotic blockade.” The former heroin addicts needed to take one oral daily maintenance dose which allowed them to function normally. In 1965, translational studies of methadone maintenance treatment involving additional patients were conducted by Nyswander at what was then Manhattan General Hospital.

Early in the research, in 1964, Kreek planned and initiated long-term prospective studies of the physiological effects and medical safety of methadone maintenance. This work was central to the approval in 1973 by the FDA of methadone for the long-term pharmacotherapy for opiate addiction. In parallel with colleagues at Cornell, Kreek also developed the first analytical technique for measuring methadone and other opioids in blood, other fluids, and tissues, which led to the documentation of the unique long-acting properties of this medication. Despite continuing public controversy over the nature of drug addiction, methadone maintenance remains an effective therapy for managing heroin and other opiate addiction and today is provided to about one million people worldwide.

Vincent P. Dole received the AB in mathematics from Stanford University (1934), and the MD from Harvard Medical School (1939). In 1941, after an internship at Massachusetts General Hospital, he joined the Rockefeller Institute Hospital as an assistant in the laboratory of Donald D. Van Slyke. During World War II he joined the Naval Medical Research Unit of the Rockefeller Institute Hospital. After a brief appointment at Harvard University Medical School, he returned to Rockefeller in 1947, and was appointed full member (professor) in 1952. The first annual award of the National Drug Abuse Conference was presented to Dole and Nyswander in 1978, and the Nyswander-Dole Award was created in 1982 by the New York Urban Coalition, the New York State Division of Substance Abuse Services, and the Committee of Methadone Program Administrators. Among many awards and honorary degrees recognizing his work, Dole received the Gairdner Foundation International Award (1972) and the Lasker Award (1988). He was an elected member of the U.S. National Academy of Sciences (1972).

Mary Jeanne Kreek received the BA from Wellesley College (1958) and the MD from Columbia University College of Physicians and Surgeons (1962). During her residency at Cornell University Medical College, she was appointed guest investigator at The Rockefeller University from 1964 to 1967. She became assistant professor at Rockefeller in 1967, head of her own laboratory in 1974, and was named professor in 1994. She was a Senior Attending Physician in the Rockefeller University Hospital and Beatrice M Haggerty Professor. She served for many years as the Principal Investigator and Scientific Director of a P-60 Research Center at Rockefeller sponsored by the National Institute on Drug Abuse, a component of the National Institutes of Health. Kreek’s achievements have been recognized with many awards and honors, including honorary degrees from the University of Uppsala (2000) and Tel Aviv University (2007), the Betty Ford Award (1996), the Special Recognition Award for Research in the Science of Addiction from the Executive Office of the President (1998), the Nathan B. Eddy Memorial Award for Lifetime Excellence in Drug Abuse Research (1999), the R. Brinkley Smithers Distinguished Scientist Award (1999), the Marian Fischman Award of the College of Problems and Drug Dependence (2003), and the Gold Medal for Distinguished Achievements in Academic Medicine of the Columbia University College of Physicians and Surgeons Alumni Association (2004).

Marie Nyswander graduated from Sarah Lawrence College (1941) and received the MD from Cornell University Medical School (1944). After completing her surgical internship she joined the U.S. Navy in 1945 and was posted to the Lexington Narcotic Hospital of the U.S. Public Health Service. She then did a residency in psychiatry at New York Medical College under Lewis Wolberg. In 1950 she established her own practice, and in 1955 helped launch an outpatient program, the Narcotic Addiction Research Project, in New York City. The next year she published The Drug Addict as Patient (1956). Nyswander was adjunct professor at The Rockefeller University from 1964 to 1986.