



# Center for Clinical and Translational Science e-Newsletter

## Center News

### Rockefeller University Partners with Community Practitioners and Institutions to Study and Eliminate Health Disparities

By Jonathan N. Tobin, PhD & Rhonda G. Kost, MD

#### Introduction

The study of health and illness in populations often begins by observing differences in patterns across person, place, and time. These differences may provide clues to sources of variation that may reflect not only biological processes, but also underlying inequities in access to resources that some groups experience relative to others. The recent focus on enhancing diversity, equity and inclusion in medical and educational institutions attempts to address these issues of biological diversity, inequities in access to healthcare and the social determinants of health (e.g., safe and attractive housing, recreational facilities,



Studies of Antibiotic-Resistant Skin Infections: Rockefeller and CDN, in collaboration with several CDN member FQHCs in NYC, Westchester, NY, and Austin, TX.

healthful food, economic stability, and access to education), and inequities in access to diverse medical professionals who provide care.

Clinical research provides an excellent lens with which to examine diversity, equity, and inclusion in access to research,

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### Emma Guttman-Yassky, MD, PhD, Rockefeller University Clinical Scholar Graduate, named Chair of the Kimberly and Eric J. Waldman Department of Dermatology at the Icahn School of Medicine at Mount Sinai

Provided by [Mount Sinai Newsroom](#)

Emma Guttman-Yassky, MD, PhD, a world-renowned expert in the molecular and cellular pathomechanisms of inflammatory skin diseases, has been named Chair of the Kimberly and Eric J. Waldman Department of Dermatology at the Icahn School of Medicine at Mount Sinai and the Mount Sinai Health System.

Dr. Guttman-Yassky is the first woman to serve as Chair of a Department of Dermatology in New York City. She is currently the Sol and Clara Kest Professor of Dermatology, Vice Chair of Research, Director of the Center for Excellence in Eczema, and Director of the Laboratory of Inflammatory Skin Diseases at Mount Sinai. She will retain her Center and Laboratory roles after her new appointment.

Board certified in dermatology in the United States and Israel, Dr. Guttman-Yassky earned her medical

degree from the Sackler School of Medicine at Tel Aviv University, and her PhD from Bar-Ilan University Ramat-Gan, both in Israel. She joined Dr. James Krueger's Laboratory of Investigative Dermatology at Rockefeller after completing a dermatology residency at the Rambam Medical Center/Technion Institute in Haifa. During her Clinical Scholar training she studied psoriasis and atopic dermatitis. After graduating, she performed a second dermatology residency at Weill-Cornell Medicine in New York. She then joined the Icahn School of Medicine faculty in 2011 upon completion of her training.

"I am both excited and humbled by the opportunity to serve as System Chair for the Department of Dermatology at Mount Sinai," said Dr. Guttman-Yassky. "Dr. Guttman-Yassky one of the leading experts in inflammatory skin diseases and authored more than 275 articles. Her research on atopic dermatitis/eczema has contributed to many of the recently

developed treatments for this disease. She has also shown that AD is a complex disease with distinct phenotypes based on ethnicity, age, and other factors, with



Dr. Guttman-Yassky & Dean Dennis Charney

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# NYC Chapter of the International Association for Clinical Research Nursing (IACRN) & The Heilbrunn Family Center for Research Nursing host an Educational Program on the Health and Research Needs of the Transgender Population

By Rita Devine, MPA, RN



Rita Devine, MPA, RN, President, ICRN NYC Chapter



Bernadette 'Candy' Capili, PhD, NP-C, Director, Heilbrunn Family Center for Research

Although there is a strong perception by researchers that there is a lack of representation from members of the transgender community in clinical research, there are few data on their actual representation in clinical trials. Approximately 2 million people in the United States identify as transgender and they have specific health needs that are not currently adequately met. Thus, there is a need to educate health care providers and staff about transgender physical and mental health, as well help health care providers and staff develop cultural competencies (defined as a range of cognitive, affective, and behavioral skills

that lead to effective and appropriate communication) so that they are better able to serve this community.

On Tuesday September 14, the NYC Chapter of the International Association of Clinical Research Nurses (IACRN) together with the Heilbrunn Family Center for Research Nursing hosted the webinar "Making Clinical Research Transgender Inclusive." This webinar presented to clinical research nurses an introduction to the transgender community. It highlighted important information and strategies for the inclusion of transgender individuals in clinical research. The speakers were

staff members from the Gender Multi-specialty Service at Boston Children's Hospital and clinical research staff from Massachusetts General Hospital. Kate Millington, MD, an attending physician and Mar Barrera, BA, a clinical research assistant from Boston Children's Hospital and Mary Larkin, RN, MS, Nurse Director and Mallory Hillard, MSN NP AGPCNP-BC Nurse Practitioner from Massachusetts General stressed the importance and urgent need for readily available and accurate information about transgender physical and mental health needs. The transgender community needs should be included in Cultural Competencies training programs that are commonly required in health care facilities. A highly interactive question and answer session with the 68 attendees followed the presentations, moderated by Elizabeth Ness, MS, RN from the NIH/NCI and an IACRN member.

## Positive Exposure

By Editorial Staff

As part of the Clinical Scholars program's Humanities in Medicine initiative a group of Clinical Scholars visited the POSITIVE EXPOSURE gallery in New York City. POSITIVE EXPOSURE was founded by Mr. Rick Guidotti, an award-winning fashion photographer, who has brought his artistry to photographing individuals with genetic disorders. POSITIVE EXPOSURE promotes a more inclusive world through award-winning photography, films, exhibitions, lectures and educational programs. For nearly

25 years, POSITIVE EXPOSURE has collaborated globally with nonprofit organizations, hospitals, medical schools, educational institutions, and advocacy groups to promote a more equitable and compassionate world where individuals and communities at risk of stigma and exclusion are understood, embraced, and celebrated. The Clinical Scholars toured the wonderful photographs in the gallery and watched a documentary about POSITIVE EXPOSURE's mission and programs, followed by a lively discussion with Mr. Guidotti on the opportunities and benefits of using art as a lens into viewing illness. Mr.

Guidotti has lectured at many hospitals and medical schools about how he tries to build individual self-esteem through beautiful photographs. His photographs and videos of patients and families provide a rich resource for both the science and humanities related to medicine. The interviews and testimonials from patients and their family members were especially heartwarming and inspirational. POSITIVE EXPOURE's mission can be summed up in their motto, "Change how you see, See how you change."



Redefining Beauty. Life Magazine article about Rick Guidotti's photographs of patients with albinism



Drs. Barry Coller, Bobbi Coller, Rashid Rumah; Mr. Rick Guidotti; Drs. Emre Mordeniz, and Rachel Kimani





# Publication and Dissemination: The Rockefeller Team Science Initiative

By Roger Vaughan, MS, DrPH

As a result of a three-year effort, partly funded by a CTSA Supplemental Award, The Rockefeller Center for Clinical and Translational Science (CCTS) created and published the initial results from their [Team Science Leadership Initiative in the Journal of Clinical and Translational Science](#). Moreover, CCTS has shared the team science leadership competencies and companion survey with the CTSA Hubs at Columbia University and Yale University for their implementation and use.

One of the primary goals of the CCTS Clinical Scholars Program is to help early-stage translational scientists mature into successful team science leaders. As such, “leadership” (of their projects, of a lab, of teams, of peers, in the discipline) is an important construct tended to by their mentor, and by their senior professors, colleagues, and collaborators. Strong leadership is a crucial component of team science success. Thus, we believe that ensuring that our trainees are excellent leaders will help expedite the discovery process. After reviewing the literature and assessing the views of educators at Yale and the University of Pennsylvania, the senior leadership of the CCTS developed a series of team science leadership competencies, organized under five domains. The competencies were then included in a Team Science Leadership survey designed to help trainees develop and document the achievement of their team science leadership skills during the program. Entering Scholars complete a self-evaluation using the survey that helps them understand the

## The Rockefeller Team Science Leadership training program: Curriculum, standardized assessment of competencies, and impact of returning assessments

Roger Vaughan<sup>1</sup> , Michelle Romanick<sup>1</sup>, Donna Brassil<sup>1</sup>, Rhonda Kost<sup>1</sup> , Maija Neville-Williams<sup>1</sup>, Riva Gottesman<sup>1</sup>, Rita Devine<sup>1</sup>, Prasanth Manukonda<sup>1</sup>, Andrea Ronning<sup>1</sup>, Barbara O’Sullivan<sup>1</sup>, Bernadette Capili<sup>1</sup>, Robert Macarthur<sup>1</sup> , Jonathan N. Tobin<sup>1,2</sup>, Tesheia Johnson<sup>3</sup>, Eugene D. Shapiro<sup>3</sup>, Emma Meagher<sup>4</sup>, James Krueger<sup>1</sup>, Sarah Schlesinger<sup>1</sup> and Barry S. Collier<sup>1</sup> 

competencies they need to develop to be successful team science leaders and to mark a starting point form which they can assess their progress during the program.

Mentors, Mentor designees, and senior colleagues use the survey to assess the current status of each Scholar across the five domains. Leadership assessment results for each Scholar are combined across mentor and colleague ratings, and then are verbally (and in a written summary of the findings) returned to the Scholar by the Scholars’ Mentor, the Program Director, Dr. Sarah Schlesinger, and the program co-director, Dr. Barry Collier, as part of their progress review. The five essential Team Science Leadership domains include: 1. Foundational Leadership Competencies; 2. Professionalism Competencies; 3. Team Building and Team Sustainability; 4. Appropriate Use of Resources and Execution of Study; and 5. Regulatory Accountability. The Scholar independently assesses her or

his attainment of the competencies and these ratings are compared to those of the Mentor and senior leadership. When there are major differences, these are discussed in detail. The goal is to use the survey results to stimulate discussion of the Scholar’s current status and to plot a course that will ensure that the Scholar feels that she or he has mastered the competencies by the time of graduation from the program. The results of the survey also help to identify ways in which to improve the program’s training in team science leadership as part of the program’s commitment to continuing quality improvement.

## Maija Williams, MPH Receives the 2021 American College of Healthcare Executives Regent Award

By Editorial Staff



Maija Williams, the Center for Clinical and Translational Science Administrative Director, was selected to receive the 2021 American College of Healthcare Executives (ACHE) Regent Award for Volunteer Executive. This award goes to a member of the American College of Healthcare Executives who in their volunteer efforts demonstrate a commitment to their ACHE regional chapter, Healthcare Leaders of New York (HLNY). Ms. Williams is also acknowledged for her dedication

to the HLNY Diversity & Inclusion chapter work, and as a board member of National Association of Health Services Executives, New York Regional Chapter, and her commitment to the American Public Health Association. Ms. Williams will accept her award on October 20th at the HLNY Annual Gala and Award Presentation.

## New Pilot Grants Awarded

By Editorial Staff

The Rockefeller University Center for Clinical and Translational Science (CCTS) and the Shapiro-Silverberg Fund for the Advancement of Translational Research supported 24 pilot projects out of a total of 27 applications that were submitted this year. CCTS Clinical Scholars received 10 pilot awards. This year's total of \$475,000 awarded brings the grand total of pilot project funding to \$10,988,712 since the program began under the initial CTSA grant in 2006. A total of 530 different pilots have been funded in 48 different laboratories.

### Support from the Center for Clinical and Translational Science

Pilots Projects Led by CCTS Clinical Scholars

**Amichai Berkovitz** (Simon Lab): *Genome Wide Association Studies in Fibrolamellar Carcinoma*. We are proposing a Genome Wide Association Study (GWAS) for Fibrolamellar hepatocellular carcinoma (FLC). Patients with FLC have a deletion in one copy of one chromosome which results in a fusion gene. We have shown that forcing that deletion, with CRISPR/Cas9, can produce the tumor. We will study the genomes from healthy cells of FLC patients to probe for genetic variations that are associated with these variations in disease behavior and treatment-response. This work could help guide patient management and therapeutics.

**Charlie Buffie** (Brady Lab): **Identification of Intestinal Microbiota-Derived Small Molecules that Modulate Mammalian Toll-Like Receptor Activity**. Innate immune signaling via Toll-like receptors (TLRs) influences a broad range of human physiology and disease. Native intestinal commensal bacteria modulate TLR signaling, playing roles in immune defense against intestinal pathogens, autoimmune disease, and vaccine efficacy. However, the repertoire of TLR ligands produced by these bacteria and the precise bacterial sources of such ligands is not known. Here we propose to determine the chemical identity, bacterial sources, and human intestinal abundance of TLR-active metabolites produced by native intestinal bacteria. This work may identify novel metabolites and their parent bacterial strains prevalent among the intestinal microbiota that influence human health through TLRs signaling.

**Nicole Cruz** (Roeder Lab): *Rewiring of the PPAR $\gamma$  Transcriptional Network in Monocytic Acute Myeloid Leukemia (AML)*. We aim to uncover the pathways involved in the differentiation block of monocytic AMLs hoping that it will inspire the design of successful differentiation therapies for this terrible disease. A reasonable candidate pathway to induce differentiation in AML involves signal initiation through generation of the PPAR $\gamma$ :RXR heterodimer. This proposal aims to fill this gap by applying several genomic and biochemical techniques to unearth the key players in the “rewired and leukemogenic PPAR $\gamma$  transcriptional network”.

**Katherine Knorr** (Ravetch Lab): *Defining Expression of Fc Receptors in Acute Myeloid Leukemia*. Despite nearly five decades of research aimed to advance therapy for acute myeloid leukemia (AML), many patients do not respond to chemotherapy or newly approved targeted agents. Primary refractory disease as well as relapsed disease are not only difficult to treat but confer dismal patient prognosis with overall survival measured in months. There is a clear need for novel or alternative therapeutic approaches for patients with aggressive, difficult to treat disease. The goal of this project is to profile expression of Fc receptor across immune cell populations in AML patient bone marrow toward informing rational design of optimized antibodies for AML therapy.

**Dennis Schaefer-Babajew** (Nussenzweig Lab): *Effects of Passive mAb Administration on Subsequent Adaptive Immune Responses to Cognate Antigen*. Antibodies are thought to be the primary active compound responsible for the protective effects elicited by challenge with antigen, such as in vaccination or infection. Additionally, the clinical use of monoclonal antibodies (mAbs) has been thoroughly established as a pillar of modern medicine in recent years. In this study, we propose to comparatively assess different aspects of adaptive immunity following vaccination against SARS-CoV-2 in individuals who previously received a combination of two potentially neutralizing SARS-CoV-2 antibodies, C135 and C144 (NCT04700163). Beyond its conceptual value in elucidating our understanding of basic humoral immunobiology, this work should also establish whether prior administration of monoclonal antibodies has any deleterious or advantageous effects for the recipient when faced with a secondary antigenic challenge, be it infection or vaccination

### Pilots Projects Led by Faculty and Postdoctoral Fellows

**Timothy Kenny** (Birsoy Lab): *Examining the Role of Mitochondrial Glutathione in Organismal Metabolism and Non-Alcoholic Steatohepatitis (NASH)*. Glutathione (GSH) is a small molecule thiol conserved throughout eukaryotic evolution. GSH is produced in the cytosol but abundantly present in other organelles such as the mitochondria. Our previous work identified SLC25A39 as the mitochondrial GSH transporter and demonstrated that loss of SLC25A39 specifically depletes mitochondrial GSH. Using a recently generated mouse model, we propose to exploit this finding to study the role of mitochondrial GSH in vivo in the context of normal physiology and metabolic disease.

## New Pilot Grants Awarded continued

**Mascha Koenen** (Cohen Lab): *Thermogenic Adipose Tissue as a Regulator of Bone Quality*. Thermogenic adipose tissue has beneficial impacts on whole body metabolism in mice and humans. In contrast to white adipocytes that store excess energy, thermogenic adipocytes contribute to increased energy expenditure through uncoupled respiration. In this proposal, I will test the novel hypothesis that thermogenic adipocytes regulate bone metabolism in mice and humans through the following aims: (1) determine the impact of loss and gain of thermogenic adipocyte activity on bone remodeling in mice and (2) investigate changes in bone quality in humans with and without thermogenic adipose tissue. These studies will provide an entirely new understanding of the impact of thermogenic adipocytes on bone biology and have the potential to identify novel therapeutic targets for anabolic bone remodeling.

**Sohail Tavazoie/Mei Wenbin** (Tavazoie Lab): *Identification of Human Germline Variants that Modulate Cancer Progression*. Cancer is a leading cause of death and a major public health burden in the developed world and many developing countries. One key challenge in cancer treatment is interpatient heterogeneity, where patients with the same subtype of cancer experience distinct clinical outcome. It has long been speculated that germline genetics is one of the main contributors to the interpatient heterogeneity, but few efforts were dedicated to study it. Here I propose a systematic study to identify human germline variants that modulate cancer progression through computational analysis and experimental validation. Preliminary unbiased computational analyses have identified 18 known or novel common germline variants that associate with breast cancer or melanoma progression. This work can also provide new insights into hereditary factors' contribution to a major human disease.

**Ruisi Wang** (Simon Lab): *The Discovery of Antibody Against DNAJB1-PRKACA in Fibrolamellar Hepatocellular Carcinoma*. Fibrolamellar hepatocellular carcinoma (FLC) is an often-lethal liver cancer affecting primarily children and young adults. The disease presents with vague symptoms, and as a result, it is usually diagnosed at an advanced stage. Thus, even for those who undergo surgical resection, there remains a high rate of recurrence. There is a lack of both existing diagnostic tests and systemic therapies; hence FLC has an overall poor prognosis. We have found that the one recurrent alteration in the genome is a somatic deletion that is only in the tumor tissue of ~400kB that produces a chimeric transcript, DNAJB1, fused to PRKACA, expressed in all tumor samples but not in adjacent normal liver. We have also shown that the expression of this chimeric protein is sufficient to produce the disease. We can detect antibodies that recognize DNAJB1-PRKACA, but not either of the parental molecules, from the plasma of patients with FLC. We sort the PBMCs isolated from patients to collect B cells, which are secreting DNAJB1-PRKACA specific antibodies. We aim to screen, identify, sequence and express patient-derived antibodies against the chimeric fusion protein.

**Zhaoyue Zhang** (Friedman Lab): *Regulation of Feeding by Dietary Fat*. Food intake and body weight are regulated by an array of hormonal and metabolic signals. The role of hormones has been confirmed by genetic and physiologic studies while the role of metabolic signals is suggested by the effect of dietary changes on weight. I now propose to study the mechanism of how these different dietary fats regulate feeding and metabolism by combining a set of biochemical, metabolomic and neurobiologic techniques. This study will have the potential to deepen our knowledge of how a ketogenic diet exerts its effect and potentially optimize it, as well as, revealing how it reduces feeding and improves metabolic regulation.

## 2020 Heilbrunn Nurse Scholar, James Muchira, Selected as the American Academy of Nursing Jonas Policy Scholar

By Bernadette Capili PhD, NP-C



Dr. James Muchira, an assistant professor of Nursing at Vanderbilt University School of Nursing, has been named an American Academy of Nursing Jonas Policy Scholar. This program, funded by Jonas Philanthropies,

supports early-career scholars seeking to build their knowledge and aptitude in health policy, the policy processes, and the interconnection of politics. The program enables scholars to connect and collaborate with expert nurse leaders on the academy's health policy priorities.

As a maternal health expert, Dr. Muchira studies how cardiovascular risk is transmitted from parents to children. He received the Heilbrunn Nurse Scholar Award to investigate the association between maternal ideal cardiovascular health and childhood obesity among children aged 1-5 years. His current research focuses on the effect of maternal stress and arterial stiffness on early risk factors and epigenetic markers of cardiovascular disease in young children. Dr. Muchira is among

six fellows participating in the fellowship. Over two years the scholars will engage in direct policy actions that align with the academy's policy priorities: advancing health equity and championing wellness, promoting innovation and sustainability, and reducing patient, provider and system burden. Fellows are mentored by members of the American Academy of Nursing National Policy Mentoring Committee and work closely with the senior director of policy and policy assistant to promote the academy's vision to impact and influence health policy. Fellows also participate in an immersion program in Washington, D.C., interacting directly with partner organizations and policymakers at the federal level to foster change-making relationships.

## 2014 Heilbrunn Nurse Scholar Alumna, Jessica Castner, Selected as the National Academy of Medicine Distinguished Nurse Scholar-in-Residence

By Bernadette Capili PhD, NP-C



Jessica Castner, PhD, RN-BC, FAEN, FAAN, a 2014 Heilbrunn Nurse Scholar alumna, has been selected as the 2021-2022 National Academy of Medicine (NAM) Distinguished Nurse Scholar-in-Residence. The program is a year-long immersion experience for an American Academy of Nursing Fellow to enhance their expertise and play a prominent role in developing health policy at the federal level while engaging in interprofessional

collaborations with scholars at NAM.

NAM is a premier institution that provides evidence-based solutions and offers comprehensive policies to advance public health and address health inequities, such as the recently report *Future of Nursing 2020-2030: Charting a Path to Achieve Health Equity*. NAM catalyzes critical health issues to the forefront of the public eye and policymakers' agendas through reports and other activities. In addition, the Distinguished Nurse Scholar-in-Residence position provides crucial nursing perspectives to support better public health.

Dr. Castner is the President and Principal Investigator/Consultant of Castner Incorporated and Editor-in-Chief of the *Journal of Emergency Nursing*. An expert in emergency and environmental health, Dr. Castner hones her clinical, entrepreneurial, and research experience to develop the next generation of telehealth and emergency care that understands and addresses

social determinants of emergency medicine utilization to create more equitable care. Her pioneering work to integrate environmental health research, emergency nursing, and data science modeling within a social justice framework has enabled her to promote healthy environments and prevent health emergencies.

Dr. Castner indicated that she will use this opportunity to impact nursing's role in environmental justice and the future well-being of our nation. She will also maximize her opportunity for interprofessional collaboration to continue her work on environmental health equity initiatives. The Heilbrunn Family Center is proud of Dr. Castner and her accomplishments. Her selection to this prestigious program is a graphic example of nursing excellence that bridges contemporary nursing practice with health policy.

## Emma Guttman-Yassky, MD, PhD - continued

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important therapeutic implications. She has recently also extended her research interest to alopecia areata in which her findings have also been translated to novel therapeutic targets. She is now testing (both clinically and mechanistically) multiple targeted-therapeutics for atopic dermatitis and other inflammatory skin diseases.

In her new role as Chair, Dr. Guttman-Yassky will continue her inflammatory disease research program focusing on eczema/atopic dermatitis



(AD), which has also recently expanded to other inflammatory skin diseases, including alopecia areata, scarring alopecia, keloids, and ichthyosis. She has developed comprehensive molecular maps of AD, defining skin differentiation and immune circuits characterizing this disease. Using a translational bench-to-bedside-and-

back approach, Dr. Guttman-Yassky seeks discoveries that will lead to novel immune pathway-specific drugs that can be tested in patients with inflammatory skin diseases.

Dr. Guttman-Yassky is co-founder and current President of the International Eczema Council, which has grown to more than 100 world leaders in eczema. She has received many national and international awards, most recently the prestigious research achievement award of the American Skin Association and she is an elected member of the American Society of Clinical Investigation.

# Meet the Scholar: Jeffrey Wong, MD, PhD

By Editorial Staff



Dr. Jeffrey Wong joined the Clinical Scholars program in July 2019 in the Leonard Wagner Laboratory of Molecular Genetics and Immunology mentored by Dr. Jeffrey Ravetch. Dr. Wong received his MD and PhD in Immunology from the University of Pittsburgh. He completed his internal medicine residency at Brigham and Women's Hospital/Dana-Farber Cancer Institute. He is currently completing a fellowship in medical oncology at the Memorial Sloan Kettering Cancer Center (MSK) with a special focus on genitourinary malignancies.

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

I was always fascinated by the elegance of biology, even as a kid. I can remember, for instance, reading this picture book called "DNA is Here to Stay" that had little drawings of cells and animals and smiling kids with magnifying glasses. I was astonished by the thought that these tiny, lettered strands held the blueprints for everything from elephants to coconuts - even me - and that by understanding this code you could figure out how it all worked. During high school, as my interest in science matured, I became especially fascinated by immunology and the incredible specificity, efficiency, and durability of our body's own immune system to detect and fight disease. At the same time, though, I wondered how and why these seemingly perfect processes, described so neatly in the textbook, could fail. I was fortunate at that point to be introduced to a lab asking just these types of questions (and was willing to have a high school student fumble around at the bench for a summer), which was the start of my more serious pursuit of research.

## **How did you come to Leonard Wagner Laboratory of Molecular Genetics and Immunology?**

After finishing my MD/PhD training at the University of Pittsburgh and my Internal Medicine residency training at Brigham and Women's Hospital in Boston, I was excited to come to New York for my medical oncology fellowship training at MSK.

I was especially excited because MSK's fellowship program provides significant protected time to pursue research, and through the Tri-Institutional partnership, I could tap into the incredibly rich intellectual and research environment shared between Rockefeller University and MSK. Like many others, I have always admired Dr. Jeffrey Ravetch's truly transformative work defining our fundamental understanding of antibody responses in health and disease. When I first met with him, though, I was also struck by his vision not only in pursuing groundbreaking discovery science, but also in asking important translational questions highly relevant to human health, which were of great interest to me as a physician-scientist. Combined with his impressive mentorship record and the incredible support and environment of the lab around him, I knew I wanted to join Jeff's lab for my training as part of the MSK fellowship and Clinical Scholars programs.

## **What is your current research?**

My current research focuses on understanding aspects of antibody immunobiology and how it can be harnessed to develop better anti-cancer therapeutic antibodies. We are particularly interested in the antibody Fc domain, which can play a critical role in determining the ultimate activity of a specific antibody through its pattern of Fc receptor engagement on different immune cells. By understanding aspects of this natural biology, we can also use this knowledge to rationally engineer the Fc domain to produce more effective therapeutic antibodies. For instance, I have worked heavily with agonistic antibodies targeting the immunostimulatory CD40 pathway, which is a central pathway driving productive anti-tumor immune responses. Using our understanding of the Fc domain's key role in determining the activity of CD40 antibodies, we have been able to design antibodies with significantly enhanced anti-cancer activity. During my time here, it has been incredibly satisfying to take this process truly from the bench to the bedside, studying immune mechanisms and novel engineered antibodies in sophisticated humanized mouse models and subsequently developing an investigator-initiated phase I clinical trial in partnership with MSK to translate one of these novel antibody candidates into the clinic to treat patients with bladder cancer.

## **What were your expectations when you joined the CS program and have they been met?**

I expected to receive great training on every stage of the translational research process. This has been fully met by the Clinical Scholars program, whether through direct mentored

experiences (such as in preclinical science and development of a phase I clinical program) or through workshops, didactics, and other experiences extending all the way from early-stage trial design to population-level outcomes research.

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

The value of exposure to ideas, research, techniques, etc. outside of my field is something I am reminded of frequently. Too often, it is easy to become hyper-focused because of the incredible body of knowledge that is out there even in one narrow area. Through interactions with my fellow Scholars, many of whom are working in quite different fields, and by participating in events like the Scholars Tutorials and the Seminar in Clinical Research, I am reminded how rich these diverse experiences can be and how it can directly strengthen my research in often unexpected ways.

## **What has been the most educational, interesting, and/or surprising aspect of being in the CS program?**

Taking a novel therapeutic concept "soup to nuts" all the way from preclinical lab studies to an early-phase clinical trial (and using the data and biospecimens from that trial to feed back to lab science and the design of future clinical studies) has truly been the most educational, interesting, and rewarding aspect of my time in the program. Along the way, I have learned so much from an incredibly large group of mentors and collaborators, from Jeff and my lab group on the preclinical side to my clinical mentors at MSK and so many more (biostatisticians, clinical research support teams, regulatory specialists, pharmacists, intellectual property experts, etc., etc., etc.). It has been a transformative experience that I will carry with me throughout my future career.

## **If you someone asked you to describe the CS program in one sentence, what would it be?**

I think that my colleague and former Clinical Scholar Ohad Bentur said it best, that the Clinical Scholars Program "teaches you to learn how to conduct research the right way."

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

After I graduate, I plan on applying what I have learned in the Clinical Scholars Program and my training as a physician-scientist toward a career at the interface of understanding and engineering the immune system for novel cancer therapies.

which includes both the composition of the research team, and the “external validity” or generalizability of research findings across the broad range of those at risk of a particular disorder. This leads to the questions: (1) are the researchers, themselves, representative of the diverse populations they study care for, and (2) are the eligibility criteria and the design of the study optimal to encourage participation by a diverse population of individuals reflecting those who are most affected by the disorder? Thus, the research study itself can become a vehicle for enhancing equity.

## **Community Engaged Research at The Rockefeller University Center for Clinical and Translational Science**

The [Community Engaged Research \(CEnR\) Core](#) at The Rockefeller University Center for Clinical and Translational Science (CCTS), which has been funded by an NIH Clinical and Translational Science Award (CTSA) since 2006, routinely addresses these issues by engaging a broad range of stakeholders in the design, conduct, analysis and dissemination of research conducted by teams formed at the CCTS. This approach to developing community partnerships has led to a number of interesting and important research and training collaborations, where Rockefeller, in partnership with different types of community organizations, has been able to reach populations that are systematically excluded from research, both as investigators and as research participants.

The CCTS is committed to developing community-academic research partnerships that engage under-represented and marginalized populations into the clinical and translational research enterprise, broadening the scope of questions that are studied by these research collaborations, enhancing the diversity of the participants and the audiences where the results are disseminated, and setting in motion the opportunity to observe the implementation, scale-up, sustainability and public health impact of these research collaborations, while simultaneously discovering the basic mechanisms underlying these sources of variability, a hallmark of Rockefeller research.

In 2006, CCTS partnered with Clinical Directors Network (CDN), a

primary care practice-based research network (PBRN), clinician training organization, and an AHRQ-designated Center of Excellence (P30) for practice-based research and learning. CDN works with Federally Qualified Health Centers (FQHCs) and other primary care safety-net practices across the USA, in partnership with its “Network of Networks,” the CDN N2-PBRN, which includes twelve PBRNs and several other clinical data networks. These clinical service organizations are often led by practitioners who are master clinicians but may lack the methodologic training to turn their unanswered clinical questions into robust and testable hypotheses. While PBRNs such as CDN are highly successful in addressing epidemiologic and health services-related questions that fall along the community-based and public health (T3/T4) side of the translational research spectrum, they often lack the expertise to ask basic science/mechanistic questions, which are considered the T0/T1/T2 side of the translational research spectrum. Herein lies a great opportunity of partnering T0/T1/T2 investigators through team science with T3/T4 investigators, thus obtaining the synergy that can come from a full spectrum approach.

## **Studies of Antibiotic-Resistant Skin Infections**

Rockefeller and CDN, in collaboration with several CDN member FQHCs in NYC, Westchester NY and Austin TX, have enrolled patients in several research studies who are receiving care for skin and soft tissue infections (SSTIs) produced by antibiotic-resistant bacteria (MRSA). These infections are challenging for clinicians to manage and very distressing and potentially very serious for patients, especially when they lead to blood-stream infections. These comprised the Community-Associated MRSA Project (CAMP) and included laboratory investigators from Dr. Alex Tomasz’s basic science lab at Rockefeller, CCTS clinical research facilitators, epidemiologists and health services researchers from CDN, practicing clinicians from CDN member FQHCs, and a range of community advisors including a barber (who routinely sees SSTIs on the scalp and neck of customers), a community pharmacist, as well as patients and caregivers who had the lived experience of having infections

caused by MRSA. Together, the research team, which involved two clinical scholar alumnae, Teresa Evering MD MSc (Markowitz Lab/Aaron Diamond Institute) and Mina Pastagia MD MS (Fischetti Lab), identified and reported on infection-related disparities between study participants who were USA-born, who were more likely to have an SSTI caused by MRSA and those who were born outside of the USA, who were more likely to have an SSTI caused by a similar bacterium that was not resistant to antibiotics. Initial results suggested that participants born in the USA may have had greater lifetime exposures to antibiotics as one potential explanation for the observed difference.

Patients with MRSA infections often have recurrences even after effective treatment and so the group decided collectively to seek funding for a clinical trial to study which factors predict SSTI recurrence, and what interventions can prevent SSTI recurrence and household transmission. The grant proposal was successful and funding for the study came from the Patient Centered Outcomes Research Institute ([www.PCORI.org](http://www.PCORI.org)) These questions, spanning basic science through global public health and environmental science, emerged organically as the team explored the implications of the data collected in the initial study. Ongoing CAMP studies are now examining the clonal diversity of the pathogens, the microbiomes of both the skin and homes where patients live, as well as whether geography and social networks can explain the geospatial distribution of the disease in the communities at risk.

## **Studies of Cardio-metabolic Risk Among Adolescent Women in NYC**

With funding provided by CCTS pilot studies, the Center for Biomedicine and Nutrition at Rockefeller and the New York Academy of Sciences, CDN and Rockefeller brought together the clinical leaders from a prior NIH-funded cluster randomized clinical trial conducted by CDN to reduce the incidence of low birthweight babies delivered by African American and Latina teenagers in NYC. The clinicians, who were drawn from CDN-member FQHCs and community hospitals, wanted to learn more about their patients’ risk factors. Using data that



is generated during routine patient care (“real world data”) to generate a better understanding of disease (“real world evidence”) is an important component in building a “learning healthcare systems.” The study focused on examining the associations between obesity and cardiometabolic risk factors, including blood pressure, blood lipids and blood glucose, and pregnancy outcomes. The Rockefeller-CDN-Health Care Team carefully extracted information from the six participating health systems and these data were then analyzed by experts in metabolism, informatics, biostatistics and epidemiology. Together with the practicing clinicians, they demonstrated that obesity correlated with less healthy cardiometabolic parameters, including blood pressure, cholesterol levels, and blood glucose. A follow-up study extracted data from electronic health records for care provided to similar young women at academic health centers in New York City through the INSIGHT Clinical Research Network. Analyses conducted by Dana Bielopolski MD PhD, a Clinical Scholar and Carolyn Jiang MS, a biostatistician, demonstrated identical statistically significant trends, but with one strikingly troublesome difference: the impact of obesity on unfavorable cardiometabolic determinants of health was greater for young women receiving health care at FQHCs as compared to those receiving care at academic health centers in NYC. The difference between these effects is an important measure of health disparities, as the women seen in FQHCs are more likely to be low income and either African American or Latina as compared to women seen in the academic health centers. Both studies emphasize the importance of “bending the cardiometabolic curve” as the babies born to overweight and obese mothers had higher birthweights, which other studies indicate will make the babies more likely to experience greater cardiometabolic risk as they age. This multigenerational effect probably contributes to the disparities in cardiovascular incidence and mortality rates between blacks and whites reported in national and state data systems.

## Studies of Cardiovascular Risk Factors Among Older Adults

In a different type of community-academic partnership, CCTS and CDN partnered with the [Carter Burden Network](#) (CBN), a community-based provider of senior services, including

meals for food-insecure older adults aging in place in NYC. CBN was interested in partnering with Rockefeller-CDN to design an evaluation study to assess the impact of CBN’s nutritional programs on their participants. After CCTS and CDN staff developed a relationship with the CBN staff and attendees, a CCTS-supported pilot study found high rates of uncontrolled hypertension among the predominately low-income minority food-insecure older adults who come regularly to CBN for congregate meals, food pantry access, health education, and other community services. Uncontrolled hypertension is a major contributor to the disparities in cardiovascular disease and mortality among older adults in communities at risk.

To address this challenging problem the Rockefeller-CDN-CBN team created novel nutritional programs for community-residing seniors to test two evidence-based interventions to achieve better blood pressure control: (1) implementing the Dietary Approaches to Stop Hypertension (DASH) diet, which is designed to decrease sodium and saturated fat intake and increase potassium, dietary fiber and mono-unsaturated fat intake, and (2) providing home blood pressure monitors (HBPMs) and training in how to use and record blood pressures taken at home. Participants had the opportunity to try new foods and new preparations and were invited to provide feedback as the meals were adjusted.

COVID-19-related closures of communal meal sites required creativity and so the study changed to providing “grab-and-go” DASH meals. Preliminary analyses demonstrate a signal of systolic blood pressure reductions that encourage us to think that when optimally employed it will be both effective and sustainable.

Unique aspects of this partnership included bringing together the scientific and clinical expertise of Rockefeller bionutritionists with the chefs, food preparers and servers at CBN, along with the oversight and approval of city governmental agencies (NYC Department for the Aging and NYC Department of Health and Mental Hygiene). A parallel mechanistic study funded by a CCTS pilot grant and the National Kidney Foundation, also led by Clinical Scholar Dr. Dana Bielopolski, involves African American participants with elevated blood pressure who are admitted to the Rockefeller University Hospital, where they are fed the DASH diet, and their blood pressure, kidney-related hormones (renin and aldosterone), electrolytes (sodium, potassium), and urinary exosomes are closely monitored to understand the underlying mechanisms that contribute to the clinical effectiveness of the DASH diet. Thus, this project truly is full spectrum in including basic research and a clinical trial with profound potential implications for public health policy.

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Studies of Cardio-metabolic Risk Among Adolescent Women in NYC: The Center for Biomedicine and Nutrition at Rockefeller and the New York Academy of Sciences, CDN, and clinicians from CDN-member FQHCs and community hospitals.

## Conclusion

These examples of full-spectrum translational research suggest the importance of designing studies that examine health disparities and test implementation strategies from the perspectives of differences across populations (epidemiologic associations) and the underlying basic science which explains these differences (biological mechanisms). These novel community-academic partnerships bring together Rockefeller, a Clinical and Translational Science Award grantee institution with expertise in basic science, with CDN, a PBRN with expertise in designing and conducting pragmatic clinical trials

and observational studies in real-world, community practice-based settings. These partnerships provide collaborative research and learning opportunities that can enhance diversity, equity, and inclusion by engaging a broader group of stakeholders such as practicing clinicians, other service delivery providers, and patients in the research team, and by conducting studies in settings that reach underserved populations, such as FQHCs and senior centers. The studies profiled above, engage populations across the lifespan, ranging from adolescent women and their babies to seniors aging in place. In this way, we can generate new knowledge that is more broadly

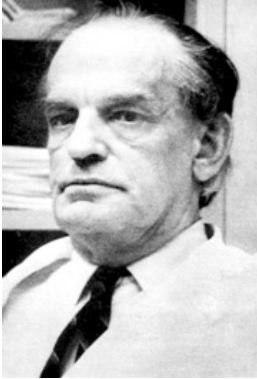
representative and inclusive, and implement that new knowledge in diverse settings reaching those most in need. A great hope for implementation science is the promise of enhancing health equity by designing and testing interventions to reduce and eliminate health disparities in the widest range of possible settings. We are always looking forward to building new basic science-to-practice research collaborations with those who share our vision and so welcome your suggestions.



Studies of Cardiovascular Risk Factors Among Older Adults: CCTS, CDN and Carter Burden Network partners.

## Rockefeller Historical Vignette: Developing a Novel Vaccine Against Yellow Fever That Remains Important Eighty Years Later

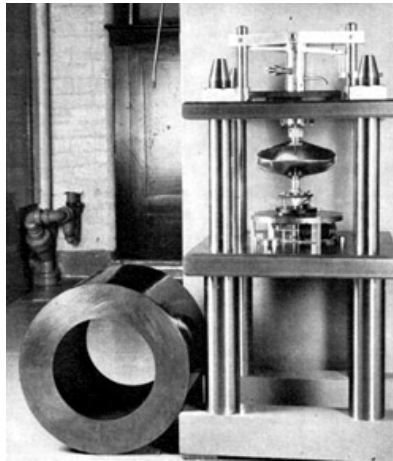
By Elizabeth (Betsy) Hanson



By 1930, the year that Max Theiler (1899-1972) arrived at the Rockefeller Foundation's International Health Division laboratories on the Rockefeller Institute campus, yellow fever was known to be a viral disease transmitted by *Aedes aegypti* mosquitoes. Controlling these mosquitoes reduced outbreaks of the disease, but a vaccine was needed to eliminate it. Theiler already was at the forefront of yellow fever research. He had disproved the claim of Rockefeller's Hideyo Noguchi that a spirochete was responsible for the disease, and he had shown that the West African and South American strains produce the same immunological response. In addition, just before moving to the Rockefeller campus, Theiler had made an important advance: he demonstrated that yellow fever could be propagated in mice. Previously researchers had used rhesus monkeys as animal models of the disease, but with mice—inexpensive and prolific—Theiler was poised to make rapid progress toward a vaccine.

The Rockefeller Institute was a world-renowned center for virus research in the 1930s. Theiler continued his mouse studies in the Rockefeller Foundation laboratories, finding that the yellow fever

virus became less virulent in monkeys after many passages through mouse brain. He also cultivated the virus in tissue culture, working with Eugen Haagen. Tom Rivers, an eminent virologist at the Rockefeller Hospital, had with Haagen developed an attenuated strain of vaccinia virus a few years before, for use as a smallpox vaccine, and in informal conversations Rivers had suggested this as a research path toward the yellow fever vaccine.



The ultracentrifuge used in recent studies on yellow fever. From *Yellow Fever* by Strode, G., 1951

Theiler experimented with several strains of the yellow fever virus, passing them hundreds of times in different kinds of tissue culture and testing them for the ability to attack the nervous system—a property of the virus that needed to be eliminated to make a safe vaccine. In 1937 these studies succeeded when a strain known as the Asibi strain underwent a change that rendered it harmless. This became the basis of a live vaccine of attenuated virus, known as the 17D strain, that was field tested in

Brazil the next year. Since then hundreds of millions of doses of the yellow fever vaccine have been given, and the methods for producing it have remained essentially the same as those Theiler developed. For his discoveries concerning yellow fever and how to combat it, Theiler was awarded the Nobel Prize in 1951.

Max Theiler studied at the University of Capetown Medical School, and later at the London School of Tropical Medicine, where he was awarded a diploma of tropical medicine and hygiene in 1922. That year he became a Licentiate of the Royal College of Physicians and a member of the Royal College of Surgeons, and joined the department of tropical medicine at Harvard Medical School. In 1930 he moved to the International Health Division of the Rockefeller Foundation, to a laboratory on the campus of the Rockefeller Institute. He remained with the Rockefeller Foundation, becoming in 1951 the director of laboratories of the foundation's Division of Medicine and Public Health, New York. In addition to the Nobel Prize (1951), Theiler's work was recognized by the Chalmer's Medal of the Royal Society of Tropical Medicine and Hygiene (London, 1939), the Flattery Medal (Harvard, 1945), and the Lasker Award (1949).