



# Center for Clinical and Translational Science e-Newsletter

## Center News

### Charles M. Rice, PhD receives 2020 Nobel Prize

The Rockefeller University website



Dr. Charles M. Rice, who studies disease-causing viruses and how the immune system defends against them, was presented with the Nobel medal and diploma in December at the Swedish Consulate in New York City.

Dr. Rice was announced as a recipient of the 2020 Nobel Prize in Physiology or Medicine, along with Harvey J. Alter of the National Institutes of

Health and Michael Houghton of the University of Alberta, in October.

Because of the COVID-19 pandemic, the 2020 laureates received their Nobel diplomas and medals in their home countries in lieu of traveling to Stockholm, Sweden for the traditional ceremony. The ceremonial presentations, along with a digital greeting from the King of Sweden and musical interludes, were streamed by the Nobel Foundation, as was Dr. Rice's prerecorded Nobel Lecture in Physiology or Medicine. Dr. Rice is the Maurice R. and Corinne P. Greenberg Professor in Virology and Head of the Laboratory of Virology and Infectious Disease. He was honored for research that contributed to a cure for hepatitis C. In particular, his work

helped identify and characterize the virus responsible for hepatitis C, which was commonly transmitted by blood transfusions before a test to detect the virus became available, and can lead to liver scarring and cancer. Dr. Rice's studies made it possible to grow the virus in tissue culture cells, a major breakthrough that ultimately enabled the development of new classes of drugs to treat the infection. A combination of these drugs can now eradicate the virus within weeks, curing the disease.

Dr. Rice is the 26th scientist associated with Rockefeller to be honored with the Noble Prize.

### Dr. Christian Gaebler receives The Clinical Research Forum 2021 Top Ten Clinical Research Achievement Award

By Editorial Staff



Dr. Christian Gaebler, a third-year and co-Chief Clinical Scholar in Dr. Michel Nussenzweig's Laboratory of Molecular Immunology was

selected to be one of the recipients of The Clinical Research Forum 2021 Top

Ten Clinical Research Achievement Awards for his study entitled Evaluation of the anti-SARS-CoV-2 humoral immune response in a cohort of COVID-19 convalescent individuals that was published in the journal Nature in June 2020. The Clinical Research Forum will honor Christian's clinical research study and nine other outstanding studies at the 2021 Top Ten Clinical Research Achievement Awards

Virtual Event on March 30, 2021.

In a highly collaborative project, Dr. Gaebler and a team of physician-scientists, immunologists and virologists studied the immune response to SARS-CoV-2 in over 150 volunteers who had recovered from COVID-19. Using methods to isolate individual B lymphocytes with receptors that

[continued on Page 4](#)

### From bench to bedside in 41 weeks – RUCOV1, A Phase 1 First in Human study of anti-SARS-CoV-2 antibodies at Rockefeller University Hospital

By Christian Gaebler, MD

With a green light from the FDA, a clinical group headed by Marina Caskey, professor of clinical investigation, started a Phase 1 study of a combination of two anti-SARS-CoV-2 monoclonal antibodies, C144-LS and C135-LS, in January this year.

Once again, and during the months leading up to the start of this Phase 1 study, Rockefeller University Hospital was at the heart of a truly translational journey that allowed the advancement of two newly discovered molecules with the potential to treat and prevent COVID-19

into a Phase 1 study in healthy volunteers in a span of only 41 weeks.

It all started on April 1, 2020 when the first COVID-19 convalescent participant enrolled at Rockefeller University Hospital and a group of physician-

[continued on Page 4](#)

## Maija Williams, MPH Receives the American Public Health Association Award

By Roger Vaughan, MS, DrPH



Maija Williams, The Center for Clinical and Translational Science Administrative Director, was recognized three times this fall for her outstanding contributions as she was the recipient of a prestigious American Public Health Association (APHA) award, was elected to serve as a Governing Councilor of APHA, representing the Health Administration section, and elected to serve as the 2021 Chair of the Diversity and Inclusion Committee of the Health Care Leaders of New York.

Ms. Williams was selected to receive the 2020 Health Administration Section Excellence in Health Administration Award. This award recognizes a Health Administration Section Member who demonstrates achievement in the health administration field, and who has gone above and beyond their job description to make a lasting impact in their organization or in public health. She received the award (virtually this year) at the Health Administration Section Meeting at the American Public Health Association Annual Meeting in the Fall of 2020.

Ms. Williams was also elected by her health administration peers to serve as Governing Councilor, representing the Health Administration section. The Governing Council is the representative legislative body of APHA. It consists of voting and nonvoting members who represent different constituencies within

APHA. Governing Councilors adopt policy statements, amend bylaws, adopt rules of business, and elect the Executive Board and Officers of APHA, among other responsibilities.

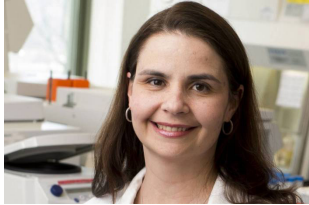
In her role as Chair of the Diversity and Inclusion committee for the Health Care Leaders of New York, she will have a leadership role in developing policies for the organization, which represents professionals in the New York Metropolitan Area, providing access to networking, education, and career development for American College of HealthCare Executives members.

Please join us in congratulating Ms. Williams on this important recognition.

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## Marina Caskey is promoted to Professor of Clinical Investigation

The Rockefeller University website



Marina Caskey, MD, a clinical scientist who leads human trials of immunotherapies for infectious disease, has been promoted to Professor of Clinical Investigation. She is a member of Michel Nussenzweig's Laboratory of Molecular Immunology.

Dr. Caskey, a clinician who joined Rockefeller as a Clinical Scholar in the lab of Ralph Steinman in 2009, has spent the last decade working on clinical studies of experimental immune-based

vaccines and therapies, particularly those for HIV. Since becoming a member of Nussenzweig's lab in 2012 she has led human trials of broadly neutralizing antibodies as a complement to antiretroviral therapy for HIV. Broadly neutralizing antibodies developed in the Nussenzweig lab, isolated from the blood cells of rare patients who successfully combat HIV without drugs, have shown tremendous promise in the trials conducted thus far; one recent study found that three infusions of a combination of two such antibodies suppressed HIV levels for an average of 21 weeks, even after antiretroviral drugs were stopped.

During the COVID pandemic, Dr. Caskey led the effort to obtain and evaluate samples of antibodies from COVID-19 patients who successfully

recovered from their illness. Selected antibodies studied under this protocol, isolated and tested for potency, have taught researchers much about the body's natural immune response to SARS-CoV-2 and have led to the development of experimental antibody-based treatments for COVID-19.

Dr. Caskey received her medical degree from the Federal University of Sergipe, in Brazil, and completed specialty training in infectious disease at Weill Cornell Medicine, where she remains an attending physician. Dr. Caskey is an alumna of the Rockefeller University Clinical Scholars program where she received a master's degree in clinical investigation and is a member of the American Society of Clinical Investigation.

# Chibuzo U. Enemchukwu, MD, MS, Clinical Scholar Graduate, Delivers 2021 Talking Science Presentation - Using Science to Advance Health Equity

By Editorial Staff



Chibuzo U. Enemchukwu, MD, MS gave the [January 2021 Talking Science series talk](#) entitled Using Science to Advance Health Equity. Talking Science is a program designed to engage high school students and their teachers through interactive lectures and demonstrations in areas of current research being conducted at the University. Dr. Enemchukwu's talk was attended by more than 543 people via Zoom, including international attendees.

Dr. Enemchukwu received her MD from the University of North Carolina-Chapel Hill, and completed her internal medicine residency at Mount Sinai Hospital in New York City, and her fellowship in infectious diseases at the Albert Einstein College of Medicine-Montefiore Medical Center. She then joined the Rockefeller University Clinical Scholars program and received a master's degree in Clinical and Translational Research in June 2019.

Dr. Enemchukwu is a Senior Research Scientist in the Hunter Alliance for Research and Translation (HART) laboratory at Hunter College. She is also a Senior Consultant at Nelu Diversified Consulting Solutions LLC., a company she co-founded that works with employers to strategize

and create inclusive health and financial benefits programs that reach an increasingly diverse workforce.

When Dr. Enemchukwu was asked what health equity means, especially during the current pandemic, she replied, "Health equity means that EVERYONE has a fair and just opportunity to be as healthy as possible. Achieving health equity requires us to acknowledge and address the social determinants that affect health, such as poverty, discrimination, and access to quality education, safe environments, and health care. The COVID-19 pandemic has called attention to many of the root causes underlying health inequities and disparities in our society. We have witnessed more COVID-19 related hospitalizations and poorer outcomes among racial/ethnic minorities and the socially disadvantaged. As scientists, we have a unique opportunity to use our science to address these inequities and ensure that our work contributes to a higher and more equitable standard of health for everyone."

The significant points from Dr. Enemchukwu's talk were:

- There is no evidence of underlying genetic vulnerability to SARS-CoV-2 among different racial/ethnic groups.
- Existing health disparities explain a large part of the differences in prevalence of chronic conditions among certain racial/ethnic minorities.
- Social and environmental factors contribute to a higher risk of exposure to SARS-CoV-2 among certain racial/

ethnic minorities, specifically Black and Latinx individuals.

One of the more pointed questions from the audience was "how can science work to achieve health equity?"

Dr. Enemchukwu's provided recommendations for action, which are:

- Recognize that health inequities exist. These inequities are largely due to social determinants rooted in a history of systemic inequality.
- Ensure that we are prioritizing and including social determinants of health indicators in our data sets.
- Work collaboratively with our larger scientific community to engage our local communities with the goals of building trust, enlisting needed resources, and improving overall health outcomes.

Dr. Enemchukwu concluded her talk with the message, "Doing the 3 things listed above can help inform policies that ensure that all communities can access context-appropriate resources that allow them to be as healthy as possible. We do not have to be scientists to start doing these things - we can all start by (1) understanding that preventable inequities around health exist, and (2) we can engage folks/communities that may not look/speak/worship, etc. like we do. Learning how different people live and experience the world is an important part."

## The Clinical Research Forum 2021 Top Ten Clinical Research Achievement Award

continued from Page 1

recognize SARS-CoV-2, and study the immunoglobulin (Ig) gene repertoire at the single cell level and characterize individual antibodies, the team was able to gain important insights into the COVID-19 immune response. By rigorously analyzing the antibodies that neutralize the virus at the genetic level, they were able to provide important information for assessing antibody responses to the many vaccines under development. In addition, these studies form the basis for developing combinations of monoclonal antibodies

that neutralize SARS-CoV-2 that can be used to prevent or treat COVID-19.

The Top Ten award-winning studies exemplify major advances resulting from the nation's investment in research to benefit the health and welfare of its citizens, and reflect the influential work being conducted by investigators at nearly 60 research institutions and hospitals across the United States, as well as at partner institutions from around the world. All nominated studies were published in peer-reviewed journals during 2020.

The Top 10 were selected based on the degree of innovation and novelty involved in the advancement of science; contribution to the understanding of human disease and/or physiology; and potential impact upon the diagnosis, prevention, and/or treatment of disease.

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## From bench to bedside in 41 weeks – RUCOV1 A Phase 1

continued from Page 1

scientists, immunologists, virologists, and structural biologists began to study the humoral immune responses of a cohort of more than 150 COVID-19 recovered individuals.

This project was led by Michel C. Nussenzweig, the head of the Laboratory of Molecular Immunology, in collaboration with Paul Bieniasz, Davide Robbiani, Marina Caskey, Theodora Hatzioannou, Charles M. Rice, collaborators at Caltech, and most importantly with the help of the entire Rockefeller University Hospital Staff, including Nursing, the Clinical Research Office, Research Facilitation Office, Research Pharmacy and many others.

Using samples collected an average of 39 days after the onset of symptoms, the initial humoral responses to SARS-CoV-2 were shown to be highly variable. However, antibodies targeting distinct epitopes on the receptor binding domain (RBD) of the SARS-CoV-2 spike protein were identified, and some of these showed in vitro half-maximal inhibitory concentrations (IC50 values) as low as single digit nanograms per milliliter.

Among the newly identified were two promising antibodies, C-135 and C-144 that showed exceptional neutralizing activities against authentic SARS-CoV-2

Early on in the COVID-19 pandemic, it became clear that passive administration of neutralizing monoclonal antibodies held great clinical promise for the prevention and treatment of COVID-19. C135-LS and C144-LS, in addition to exceptional neutralizing activities, target distinct neutralizing epitopes on the RBD of the SARS-CoV-2 spike glycoprotein and, working together, they minimize the risk of the virus mutating and developing resistance to the therapy. Therefore, both antibodies were selected for further clinical development.

During preclinical testing in animal models, it could be shown that a single infusion of C135-LS and C144-LS prevented infection with a mouse-adapted SARS-CoV-2 strain in mice. In hamsters and non-human primates, the C135-LS/C144-LS combination conferred protection and rapid improvement or clearance of infection when administered intravenously before or within 24 hours

after SARS-CoV-2 challenge.

These promising results from animal models supported the hypothesis that C135-LS and C144-LS may provide protection against infection from SARS-CoV-2 and accelerate viral clearance and disease resolution in SARS-CoV-2-infected individuals.

The first in human clinical trial launched on January 13 at the Rockefeller University Hospital to assess the safety of the subcutaneous and intravenous administration of the antibody combination in a small group of healthy volunteers.

To date 17 people have been enrolled and the study is expected to be fully enrolled by March 3, 2021.

With the Phase 1 underway, Rockefeller University has taken the next step and entered a licensing agreement with Bristol Myers Squibb to advance development of C135-LS and C144-LS with the goal to enable affordable, worldwide distribution.

# Clinical Scholars Meet with Dr. Theodora Ross, Vice President of Translational Medicine for the Discovery, Pre-clinical and Early Development at Merck Research Laboratories

By Michelle Romanick

As part of the career development component of the Clinical Scholars program, leaders in translational research are invited to meet with the Scholars to discuss their own career path and research, and to provide insights on different career options. The Clinical Scholars had the privilege to meet virtually with Dr. Theodora Ross, Vice President of Translational Medicine for the Discovery, Pre-clinical and Early Development at Merck Research Laboratories on February 1, 2021.

Dr. Ross earned her M.D. and Ph.D. degrees from Washington University in St. Louis and then did an internal medicine residency at the Brigham and Women's Hospital and an oncology fellowship at the Dana-Farber Cancer Institute. Dr. Ross stated that her career path was and is still driven by her deep interest in clinical research and developing better cancer prevention and treatment. As a physician-scientist at the University of Michigan, she

cared for women with breast cancer and investigated the basic cellular mechanisms of cancer cells and how those cells resist targeted cancer drugs.

Dr. Ross later moved to the University of Texas, Southwestern (UTSW) where she was appointed the Jeanne Ann Plitt Professor in Breast Cancer Research and H. Ben and Isabelle T. Decherd Chair in Internal Medicine. She also served as the director of the Cancer Genetics Program, developing, and applying the most innovative genetic analyses to assess patients' individual risks of developing cancer as a guide for personalized treatment. Dr. Ross continues to maintain her lab at UTSW, focusing on the mechanisms that transform normal cells into cancer cells and understanding the genetics of inherited cancers.

Based on her medical expertise and her personal experience in being a member of a family in which multiple relatives developed cancer, she authored the book, "A Cancer Family," a

comprehensive guide for people facing a genetic predisposition for cancer.

Dr. Ross encouraged the Scholars to continue to build their relationships with their current mentors, as well as develop new mentor relationships throughout their career. These relationships are extremely valuable when one wants advice about venturing into new territory or one's current research. This has allowed her to make major changes in her career beyond her comfort zone with confidence. When asked what the career advice she would offer to the Scholars, Dr. Ross replied, "Be the best at what you are doing! If you are not excited about you are doing and not enjoying the work, change!"



Dr. Theodora Ross on Zoom with Clinical Scholars and Faculty

# Cerner Electronic Health Record Project

By Prasanth Manukonda, MS, MA & Maija Neville Williams, MPH

The Rockefeller University Hospital is continuing the implementation of Cerner CommunityWorks as our Electronic Health Record (EHR). Due to the COVID-19 pandemic and restrictions in place, the 'Go-live' date has moved to the second quarter of 2021.

The Hospital is working with Cerner to test, train, and implement new interfaces. In addition to iRIS and MSK lab integration, we are working with other vendors to integrate LabCorp data and ECG results with CommunityWorks to provide a one-stop

shop for all lab results and procedures.

We are also building redundancy into these systems to reduce downtime in case of emergencies or power outages after we complete the installation. This will help us provide better services to our participants and the community.

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## Rockefeller Leads Creation of New York City Area Biostatistics Collaborative (NYC-ABC)

By Roger Vaughan, MS, DrPH



Rockefeller Biostatistics maintains a strong statistical educational component for Clinical Scholars and for the broader Rockefeller research community by combining outstanding didactic courses, online support, seminars, and individual consultations, each embedding statistical and reproducibility attributes. There is also outstanding statistical consulting, provided both in person and online, for questions about sample size calculations, statistical analysis plans for grants, and for manuscript preparation. Here too, consultations are infused with methods to support reproducibility and focus attention on clinical importance over simply statistical significance. Methods development for correlated data in biology are underway, along

with research on alternative endpoints, and causal inference methods for program evaluation data. However, because Rockefeller can only support a small Biostatistics team, we have reached out to collaborate with other Biostatistics groups for educational and analytic support in specialty statistical areas, and to develop new validated analytic methods.

To leverage the impact of our group, Dr. Roger Vaughan, Director of the Biostatistics capitalized on the existing expertise residing in each of the New York City area Biostatistics departments, by spearheading the creation of the New York City Area Biostatistics Collaborative (or NYC-ABC) in 2019. The NYC-ABC initially comprised biostatistics leaders from Columbia, Cornell, Einstein, Mount Sinai, New York University, and Rockefeller, but was expanded to include Yale University in 2020. The mission of the NYC-ABC is divided into three aims: 1- To provide a forum to share information, institutional seminars and lectures, best practices, and approaches to help

expedite outstanding translational science; 2- To create the ability to share statistical expertise and excess analytic capacity across the NYC-ABC; and 3-

To create a platform to promote and create novel methods development. The NYC-ABC has already jointly authored a poster accepted to the Association for Clinical and Translational Science, has given a joint talk at a recent statistical association meeting, and is planning collaborative methods development in several priority areas, including the analysis of data from incomplete clinical trials. The NYC-ABC has fostered a culture of shared knowledge, speeding the resolution of problematic analytic issues, solved shortfalls in personnel power, and promoted creative thinking and solutions to methodological quandaries. The Collaborative has been meeting quarterly via Zoom but plans to resume in-person meetings and promote joint conferences, symposia, and poster sessions in the near future.

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## Seminars in Clinical Research

Among the Hospital's most important forums for scholarly exchanges are its year-round weekly seminars and lectures presented by staff, fellows, students, and distinguished visiting scientists. The Seminars in Clinical Research presentations are held every Wednesday from 12 PM - 1:00 PM via Zoom until May 26, 2021. Go to <https://www.rucare.org/futureseminar.php> for upcoming seminars.

### Upcoming Seminar

**March 17, 2021**

Speaker: Luis Montaner, DVM, DPhil

Title: *Marshaling Innate and Adaptive Immunity: Clinical Implications of Recent Advances in Cure-Directed Research*

Zoom registration link: [https://rocku.zoom.us/meeting/register/tJUrC-2hrj0sHt3gkSkFAQOyKgQx\\_duBHNVP](https://rocku.zoom.us/meeting/register/tJUrC-2hrj0sHt3gkSkFAQOyKgQx_duBHNVP)

## 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 25 pilot projects out of a total of 32 applications that were submitted this year. CCTS Clinical Scholars received 9 pilot awards. This year's total awards of \$565,000 brings the grand total of pilot project funding to \$10,513,712 since the program began under the CTSA grant in 2006. A total of 47 different laboratories have received 506 pilots awards

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

Pilots Projects Led by CCTS Clinical Scholars

**Ying Wang (Birsoy Lab):** *SLC25A39 Promotes Human Terminal Erythropoiesis Through Mitochondrial GSH Uptake.* Anemia affects one-third of people worldwide and is a major cause of morbidity, and so understanding how red blood cells (RBC) are produced is important. The production of RBCs is a continuously regulated multistep process named erythropoiesis. It is known that cellular metabolism is essential for human erythropoiesis, but mechanisms underlying metabolic regulation of human erythropoiesis are not completely understood. I have evidence indicating that SLC25A39, a mitochondrial-localized solute carrier protein, is responsible for mitochondrial glutathione (GSH) uptake and is pivotal for hemoglobin production during terminal erythroid differentiation. This project aims to test the hypothesis and investigate the mechanisms wherein SLC25A39 promotes human terminal erythroid differentiation through enhancing mitochondrial GSH uptake

**Jeffrey Wong (Ravetch Lab):** *CD40 Agonism for the Treatment of Bladder Cancer.* Non-muscle invasive bladder cancer (NMIBC) is an area of significant unmet clinical need, with a large, affected patient population, high rates of recurrence and progression, and limited salvage therapy options aside from radical cystectomy. We propose a novel immunotherapy approach based on the agonism of CD40, an immune-stimulatory receptor centrally involved in activating antigen-presenting cells and downstream anti-tumor immunity.

**Rachel Niec (Fuchs Lab):** *Exploring Lymphatic Capillaries as Regulators of the Intestinal Stem Cell Niche.* Adult stem cells (SCs) within the colon persist throughout life and are essential for maintenance of intestinal function and for repair following damage or inflammation. These cells rely on specialized niches to maintain their "stemness", their self-renewal, and the ability to generate progeny cell types that comprise the epithelial barrier of the colon. These studies promise to improve understanding of colonic stem cell maintenance and function and yield new therapeutic targets for treatment of inflammatory bowel disease.

**Rochelle Maxwell (Smogorzewska Lab):** *Characterizing the Role of the Fanconi Anemia DNA Repair Pathway in the Pathogenesis of Squamous Cell Carcinoma.* Fanconi anemia (FA) is an inherited disorder caused by mutation in any of 22 currently identified genes. It is characterized by genomic instability, bone marrow dysfunction and cancer predisposition. Squamous cell carcinoma (SCC) is the most commonly diagnosed solid tumor in patients with FA and represents a major source of morbidity and mortality. We propose to study SCC's cell of origin, the keratinocyte. Given that genomic instability and defective DNA repair are defining features of FA, we hypothesize that there are intrinsic characteristics of keratinocytes carrying FA mutations that contribute to the observed clinical phenotype of accelerated SCC development and progression.

**Kareem Rashid Rumah (Fischetti Lab):** *Clostridium Perfringens Enterotoxin and Rotaviral Gastroenteritis as Candidate Triggers for Sudden Infant Death Syndrome.* Although typically expressed by barrier epithelial cells, we have observed expression of tight junction proteins, claudin 3 and junctional adhesion protein 1 (JAM1), by astrocytes residing in the mammalian brainstem respiratory center. Intriguingly, brainstem astrocytes of Sudden Infant Death Syndrome (SIDS) victims display an inflammatory phenotype indicating damage to the infant brainstem prior to accidental asphyxiation. Claudin 3 and JAM1 necessarily make these astrocytes susceptible to *C. perfringens* enterotoxin (CPE) and rotavirus respectively, as these tight junction proteins serve as receptors for these two enteric pathogens. We thus hypothesized that CPE and/or rotavirus may be environmental triggers for SIDS

### Support from the Shapiro-Silverberg Fund for the Advancement of Translational Research

Pilots Projects Led by CCTS Clinical Scholars

**Dana Bielopolski (CCTS, Kost & Tobin):** *Obesity Related Renal Damage – BSA Matters.* Measurement of renal function in healthy subjects has become a focus of interest for early detection of renal disease in the general population. Currently recommended equations to estimate glomerular filtration rate (eGFR) are highly affected by muscle mass. Based on preliminary results from a cohort of healthy young women we propose that indexing eGFR to body surface more accurately reflects renal function and should be preferred in daily practice for the obese population. This correction will improve ability to identify, intervene and prevent obesity-related renal damage.

**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

## New Pilot Grants Awarded (continued)

### Support from the Shapiro–Silverberg Fund for the Advancement of Translational Research

Pilots Projects Led by CCTS Clinical Scholars (continued)

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 TLR signaling.

**Katherine Knorr (Ravetch Lab):** *Defining Expression of Novel Acute Myeloid Leukemia Marker U5 snRNP200.* We hypothesize the U5 snRNP200 protein complex is variably expressed across hematopoietic stem & progenitor cell populations in patients with AML. The goal of this project is to profile expression patterns across these populations from AML patients and verify U5 snRNP200 as a novel target for AML treatment.

**Yael Renert-Yuval (Krueger Lab):** *A Study to Evaluate Mechanistic and Pharmacokinetic/Pharmacodynamic Characteristics of Weekly Brodalumab in Hidradenitis Suppurativa Patients.* We propose to perform pharmacokinetic/pharmacodynamic studies that will explore the binding/clearance of the IL-17 receptor to Brodalumab in different immune cells along with further investigations of the immunological milieu in patients with Hidradenitis Suppurativa. This may dissect the contribution of different inflammatory cells in Hidradenitis Suppurativa, help to identify new treatment targets and direct further investigation for the development of new therapies to treat this debilitating condition.

### Support from the Shapiro–Silverberg Fund for the Advancement of Translational Research

Pilots Projects Led by Faculty and Postdoctoral Fellows

**Nneoma Adaku (Tavazoie Lab):** *The APOE-LRP1 Axis as a Suppressor of Melanoma Metastasis.* I hypothesize that APOE inhibits melanoma invasiveness by activating an LRP1 signaling axis.

**Guadalupe Astorga (Gilbert Lab):** *Perceptual Processing in Autism. People with autism show striking differences in sensory perception compared to controls.* Although several studies have tackled this issue, there is a big gap left to understand their perception. We propose to perform psychophysical measurements in human subjects diagnosed with autism and their control group to explore their ability to detect a figure immersed in a background of increasing complexity.

**Dominic Colosimo (Brady Lab):** *Bacterial Cadaverine in Gut Inflammation: Mechanistic Studies and Therapy Development.* The human body harbors a dynamic collection of bacteria that is thought to play an influential role in health and disease. The number of reports describing molecular mechanisms by which bacteria influence host physiology continue to lag behind the enormous number of correlative studies that link the human microbiome with all matters of consequence to host health. The work proposed here will expand our understanding of cadaverine's effects in vivo and serve to develop strategies to limit cadaverine accumulation using both diet intervention and drugs targeting bacterial enzymes.

**Erin Conlon (Darnell Lab):** *Depletion of SARS-Cov-2 RNA from Saliva Using Locked Nucleic Acid Probes.* Covid-19 is a global health crisis that has far-reaching consequences for public health and the broader socioeconomic climate. Since the beginning of 2020, there has been a great demand for minimally invasive, high-throughput diagnostic testing, as well as for insights into viral mutations and their impact on clinical outcomes. In this proposal, we describe the development of methodology to deplete the SARS-CoV-2 viral RNA present in human patient saliva using antisense locked nucleic acid (LNA) probes.

**Gregory Donaldson (Mucida Lab):** *Immunoglobulin A Regulation of the Gut Microbiota During the Emergence of Inflammation-Driven Gastrointestinal Cancer.* Selective immunoglobulin A (IgA) deficiency (~1:500 people) is linked with a modest increase in risk of gastrointestinal cancer. Furthermore, colorectal cancer patients present an increased concentration of fecal IgA, which is known to play an important role in regulating the mucosal microbial community. Despite the clear connections, the role of IgA in the development or progression of gastrointestinal cancers remains undescribed. We propose studying how IgA-microbiome interactions relate to both immune and microbial interactions with gastrointestinal tumors.

**Fatma Hacisuleyman (Darnell Lab):** *Developing New Tools for High Scale and Precise Testing for SARS-CoV-2.* Covid-19, caused by severe acute respiratory syndrome coronavirus 2, SARS-CoV-2, has been declared a pandemic since March 2020. To date, nasopharyngeal-based PCR testing strategies are employed by hospitals and clinics; however, the lack of sensitivity and the long turn-around time are serious shortcomings. The tests are failing to detect low copy numbers of SARS-CoV-2, posing a threat to the healthcare provider while obtaining the sample, and are taking ~2 weeks to provide the results. To overcome these challenges, we developed a self-collected saliva test that can be shipped or couriered to a clinical lab. Our aim is to use magnetic beads to extract RNA from saliva samples with in-house developed buffers in 20 minutes and pool hundred samples to scale up our testing platform and test thousands of samples a day.

**Xiaojing Huang and Paul Cohen (Cohen Lab):** Long-term pediatric cancer survivors represent a growing population with unmet clinical needs that arise from late treatment effects, such as an increased risk of diabetes seen in patients who received total body (TBI) or abdominal irradiation. In contrast to the general population, the disease has a much earlier onset in these patients and often develops in the absence of obesity. The mechanisms linking TBI or abdominal radiation to the development



## New Pilot Grants Awarded (continued)

of metabolic dysregulation remain unknown but have been postulated to involve injury and subsequent dysfunction of the abdominal adipose depots that passively receive radiation dose during treatment. By linking the acute signatures of adipose radiation response to the chronic effects of TBI or abdominal radiation on systemic metabolism, we aim to identify target pathways for future mechanistic studies that may eventually yield therapeutic strategies to mitigate the risk of diabetes in this patient population

**Juan Osorio (Ravetch Lab):** *Role of Fc Receptors as Modulators of Tissue-Specific Activity of Anti-PD-L1 Antibodies.* Antibodies targeting the PD-1/PD-L1 axis have changed cancer therapeutics, leading to sustained clinical responses in patients with a wide variety of cancers. Despite this early success, only a minority of patients respond to this class of agents and the determinants of response are poorly understood. Several clinical factors had been associated with response to therapy and particularly, we found that site of metastasis (e.g., lymph node vs. liver) influences responses to anti-PD-1/PD-L1 blockade. In this proposal we aim to understand tissue-specific immune factors, particularly the pattern of expression of Fc receptors (FcγRs) on immune cells, as regulators of differential metastatic-site responses to anti-PD-1/PD-L1 antibodies.

**Maria Passarelli (Tavazoie Lab):** *Investigating the Role of Leucyl Aminoacyl tRNA Synthetase (LARS) in Translation Regulation of Breast Cancer Tumorigenesis.* As the second leading cause of cancer deaths in US women, breast cancer remains a prevalent cause of mortality. We examine the role of tRNAs and their regulatory molecules in cancer formation and progression. In this proposal I focus on the role of leucyl aminoacyl tRNA synthetase (LARS), a tRNA charging enzyme responsible for ligating leucine to leucine tRNAs, in breast cancer formation. The proposed work will build upon the preliminary data to define a novel tumor suppressive role for LARS in breast cancer.

**Sarah Szwed (Cohen Lab):** *The Role of Otop1 in Thermogenic Adipose Tissue in Mice and Humans.* Obesity is a highly heritable complex disease. We recently identified five novel predicted functional variants in the proton-channel Otop1 that strongly segregate with obesity across multiple families in a cohort of Turkish patients. Previously characterized in the taste bud and vestibular system, Otop1 is most abundantly expressed in brown fat, where its function has not been studied. The proposed study will explore the role of a novel gene implicated in human metabolic dysfunction that has implications for future therapeutic development

**Robert Williams (Birsoy Lab):** *Metabolic Determinants of Sensitivity and Resistance To CPI-613 In Acute Myeloid Leukemia.* Acute myeloid leukemia (AML) is the second most common type of leukemia in adults representing 32 percent of all leukemia cases. It has recently become appreciated that AML cells display oncogenic alterations that change their cellular metabolism in a manner that may be selectively targeted. We will characterize the role of glycerolipid synthesis genes in the resistance and sensitivity of AML cells to CPI-613.

**Shaopeng Yuan (Fuchs Lab):** *Leptin Receptor Blockade in Tumor-initiating Stem Cells for the Treatment of Squamous Cell Carcinoma.* Squamous cell carcinoma (SCC) is one of the most frequent solid tumors in humans and is a major cause of cancer mortality. A current unmet need in fighting these cancers is to develop new markers that distinguish benign tumors from malignant SCCs, as these differences can be exploited to advance cancer therapeutics and prevention strategies. This proposal is a proof-of-concept study to examine the therapeutic approach with my xenograft model. The novelty of my proposal is that antibodies cannot pass the blood-brain barrier efficiently and would not elicit side effects on body weight through LEPR activity in the brain during use as a systematic treatment.

**Shen-Ying Zhang (Casanova Lab):** *Single Gene Inborn Errors of Immunity Underlying SARS-CoV2-Related Multisystem Inflammatory Syndrome in Children.* Since early May 2020, a rare and life-threatening SARS-CoV2-related Kawasaki-like disease, designated by the CDC as Multisystem Inflammatory Syndrome in Children (MIS-C), emerged in communities with high rates of COVID-19. Available epidemiological data has provided compelling evidence for SARS-CoV2 being the trigger of MIS-C. This project will enable us to better understand the immunopathogenesis of MIS-C.

## Meet the Graduate: Ana Pereira, MD, MS

By Editorial Staff



Dr. Ana Pereira joined the Clinical Scholars Program at the Rockefeller University in 2011 in the Laboratory of Neuroendocrinology and was mentored by Dr. Bruce McEwen. Dr. Pereira was selected as Chief Clinical Scholar in 2013 and received her Master's degree in Clinical and Translational Research in 2014

Dr. Pereira received her M.D. from the Universidade Federal de São Paulo in Brazil. She completed her Neurology Residency at Harvard University, with sub-specialty trainings in Cognitive Neurology at Columbia University, a Post-Doctoral Research Fellowship at Columbia University. After graduating from the Clinical Scholars program, Dr. Pereira was promoted to Assistant Professor of Clinical Investigation before moving to Mount Sinai. Clinically, Dr. Pereira evaluates patients at the Center for Cognitive Health at The Mount Sinai Hospital having expertise in diagnosing and treating neurodegenerative disorders and other cognitive syndromes. Dr. Pereira is the Head of the Pereira Lab on the Neurobiology of Alzheimer's Disease and Aging at Mount Sinai and Assistant Professor of Neurology and Neuroscience at the Icahn School of Medicine at Mount Sinai.

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

I have always been interested in both Arts and Sciences. I came to neuroscience because it is a bridge between the sciences and humanities as has been pointed out by Edward Wilson and Eric Kandel before by studying and trying to understand the neurobiology of language, memory, decision-making, perception, and multiple cognitive processes. When I completed my Neurology residency, I wanted to work on Cognitive Neurology and perform research as a

physician-scientist to have a potential impact on one of the disorders that mostly affects cognition, Alzheimer's disease (AD). Affected individuals slowly and progressively lose their own identity, as key abilities that make us who we are as unique human beings, our unique cognition, is slowly lost, including memory, language, insight, etc. It is a devastating disorder and I see these patients and families in clinic, their despair, and so I would like to make progress in the field more than anything else.

Another major influence was that relatively early in my career, I worked at Scott Small's lab at Columbia University. Dr. Small is a neuroscientist and neurologist. It was so exciting to make discoveries that can contribute to knowledge and that could potentially contribute to improving human health. And Scott showed me how thrilling being a scientist could be, so I knew I wanted to be part of this enterprise.

### **How did you come to the Laboratory of Neuroendocrinology?**

Bruce, who sadly passed away a year ago, was a world-renowned scientist who made landmark discoveries in neuroplasticity and neuroendocrinology. Very importantly, Bruce was a very kind person and beloved in the scientific community. Science is a human endeavor and so I decided early on to do it with people I would enjoy the journey with. Bruce gave me a tremendous amount of freedom to work on projects I designed, and I also had to raise funds to carry them out. Looking back, I think it was very important that I had to write grants early on and strategize how to support projects, which is critically necessary to carry out long-term research programs.

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

My laboratory at Mount Sinai studies the susceptibility of glutamatergic neural circuits to synaptic changes in aging and neuronal loss in Alzheimer's disease (AD). We investigate molecularly why tau pathology accumulates in glutamatergic neurons leading to neuronal loss. Our studies involve animal models, use of postmortem Alzheimer's brain tissue, all the way to a translational program

to human clinical trials. We also study the mechanisms through which sleep disturbances can increase the risk and progression of AD. As a physician-scientist, my ultimate goal is to identify novel targets and develop therapies for AD and other neurodegenerative disorders. Clinically, I evaluate patients at the Center for Cognitive Health at Mount Sinai with a diversity of cognitive syndromes, many of them due to neurodegenerative disorders, such as AD.

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

I think one of the greatest advantages of the Clinical Scholars program is to have a considerable amount of truly protected research time. This is a privilege that is extremely hard to find in any academic institution. That was a major attraction that led me to the program along with the fact that RU is such a respected Institution with historically deep scientific discoveries in basic and translation research. Once starting the program, I realized that it was far better than expected because of the committed leadership of Barry Coller and Sarah Schlesinger who are devoted to training and supporting the next generation of physician-scientists.

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

To better understand the unique features and opportunities a physician-scientist has who can uniquely design, strategize and carry out research programs that are truly translational. Clinical Scholars at Rockefeller have amazing basic science research opportunities in world-leading laboratories that can be truly translated and tested in human research with all the support that the Rockefeller University Hospital offers. We really need to bridge Science with Medicine and a physician-scientist is uniquely equipped to do so.

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

Michelle's amazing interest in and devotion to the Scholars and the program. Barry and Sarah have made

## Meet the Graduate: Ana Pereira, MD, MS (continued)

important scientific discoveries that have led to effective therapies for human disorders and they teach you about what being a physician-scientist truly is and what we can aspire to. They also have a passion for the arts, nurturing very enriching dialogues between science and the arts, which in my view is the most exciting and uniquely human enterprise. Bobbi Collier's expertise in Art History gave the Scholars wonderful insights when we attended terrific lectures and art exhibits. I personally have an immense affinity to cross disciplines bridging the Humanities and Sciences, one of the main reasons I chose neuroscience as a field in the first place.

A pleasantly surprising part of the

program that I am very grateful for was to have received the Bernard Schwartz Physician-Scientist Award, which allowed me to explore some interesting ideas that gave me preliminary data for my first R01 application. These funding opportunities at Rockefeller, as well as the amazing Tri-Institutional Therapeutic Discovery Institute (TDI) program are extraordinary opportunities that Rockefeller offers.

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

It is a unique program committed to educating the next generation of physician-scientists who can translate

fundamental basic science discoveries to human research to the benefit of human health.

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

Make the most of all opportunities available to you from the Clinical Scholars program and Rockefeller! Enjoy the intellectual environment and the amazing lectures Rockefeller University offers. Think strategically to build on your own research program and take advantage of the funding opportunities and unique programs such as TDI and many others. And have fun doing all of it!

## Meet the Scholar: Ohad Bentur, MD

By Editorial Staff



Dr. Ohad Bentur joined the Clinical Scholars program in July 2018 in the Allen and Frances Adler Laboratory of Blood and Vascular Biology mentored by Dr. Barry Collier. He received his MD from the Technion-Israel Institute of Technology, Israel and his MHA from the Ben Gurion University of the Negev. He completed his internal medicine residency and hematology fellowship at the Tel Aviv Medical Center. He currently is a third year Clinical Scholar and serves as Co-chief Clinical Scholar.

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

Growing up I was surrounded by researchers and academics. My grandfather was a professor of chemistry, my father is a professor of civil engineering, and my uncle and aunt are both physician-scientists – all from my

alma mater in Israel, the Technion. My mother was drawn to the humanities and has a PhD in linguistics, with research focusing on computational grammar. We talked science around the dinner table, and I knew from a young age that I would pursue a career in science. Medicine seemed like the perfect way to combine my interest in the exact sciences with my desire to work with people and be able to help them, and for the “benefit of humanity” (AKA “pro bono humani,” if that’s not too pretentious). For that reason, I chose to train in the medical school at the Technion, Israel’s leading polytechnic research university. The training environment there enabled me to take my first steps in basic research in parallel to medical education and gave me the tools needed to continue with research later in my career.

**How did you come to the Allen and Frances Adler Laboratory of Blood and Vascular Biology?**

Clinical medicine, and especially patients, have a tendency to draw your full attention, but I made every effort during my early training to devote at least some of my time to research. Both my clinical and research interests led me to thrombosis and hemostasis. My mentor during clinical fellowship in hematology, Dr. David Varon, is a “platelet guy,” just like Dr. Collier, and he made the introduction between us. In parallel to clinical training, I also

completed a Masters degree in Health Administration and volunteered with a patient and public health advocacy group (Physicians for Human Rights – Israel), and those activities exposed me to the worlds of drug development, medical economics, implementation science, and patient and research participant rights – all topics that do not get enough attention when working in a typical benchwork environment. I was excited to learn that on top of the opportunity to take part in the advanced benchwork in Dr. Collier’s lab, those are topics that he holds dear.

**What is your current research?**

Like many other investigators, COVID-19 temporarily shifted my research focus. Early during the pandemic, I was offered the opportunity to run a Phase 1 study in the Rockefeller University Hospital to study whether a novel aerosolized formulation of hydroxychloroquine could be delivered safely and tolerably to patients as a potential treatment for COVID-19. Our hypothesis was that at low doses, an inhaled formulation of hydroxychloroquine, which is usually administered as an oral tablet, may achieve high enough respiratory tissue concentrations to inhibit SARS-CoV-2. My training in the Clinical Scholars program and experience with drug development working on the antiplatelet drug RUC-4, which was developed

in our lab, provided me the required skillset to complete this task. The project is now nearing completion, and the drug may move ahead for further clinical development. I look forward to going back to focusing on studies related to thrombosis and hemostasis while continuing to grow in the field of drug development.

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

I knew I was joining a unique program that combines hands-on experience in the lab, which many MDs are lacking, together with formal training in translational research and clinical investigation. The experience that I gained by working with Dr. Collier and taking part in the program surpassed my expectations and I feel well-prepared to venture ahead with my career as a better scientist and investigator.

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

The ability to take part in the RUC-4

project and to lead a Phase 1 study with a new investigational drug, all the way from the bench to study participants has been an amazing learning opportunity. Drug development is a discipline with many aspects that are not part of formal academic education and training. Participating in the Clinical Scholars program provided me with the unique opportunity to gain that sought-after experience.

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

One of the most educational aspects of being in the program is the great attention that is placed on Rigor, Reproducibility, and Reporting (R3 initiative). These three pillars of research are part of my daily work and every discussion with Dr. Collier and my colleagues in the lab, as well as part of the formal training with the program's faculty. There is a real crisis in science because of lack of adherence to R3, and it is clear that academic training has not placed enough emphasis on it.

The events of this past year, especially relating to the drug that I was studying, hydroxychloroquine, emphasize just how dangerous this crisis is – it has cost people their lives and paved the way to mistrust in science.

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

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?

I plan to go back to Israel to be with my family and hope to bring back what I have learned in the Clinical Scholars program. I am torn between my original conviction to lead a career as a physician-scientist in academia, and the vast opportunities that opened up when I was exposed to the world of drug development. I hope to find a path that combines both passions

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## Anuradha Hashemi, MPH, New Community Engagement Specialist joins the Clinical Research Office

By Editorial Staff



Ms. Anuradha Hashemi joined the Clinical Research Office at the Rockefeller University Hospital and Center for Clinical and Translational Research in the role of Community Engagement Specialist.

Ms. Hashemi will foster and develop community-engaged research collaborations among scientists at Rockefeller University and community partners. She will work with the co-directors of the Community and

Collaboration Core, Dr. Rhonda G. Kost and Dr. Jonathan N. Tobin, to develop relationships with community-based organizations, develop and participate in community-engaged research projects, and disseminate project accomplishments, events, and outcomes to a range of stakeholders. Ms. Hashemi received her Master of Public Health from the Mailman School of Public Health at Columbia University.

Prior to joining Rockefeller University, Ms. Hashemi worked in the Immigrant Health & Cancer Disparities Service at Memorial Sloan Kettering Cancer Center conducting community-based research and outreach to improve health outcomes among immigrant communities in New York City. Prior to that, she worked in Dhaka, Bangladesh at the Center for Gender and Sexuality at BRAC University, where she coordinated qualitative research projects on reproductive health.

One key goal of Ms. Hashemi's position is to develop innovative and sustainable ways of integrating

community feedback into the way that research is conducted at Rockefeller, thus increasing community engagement throughout the research spectrum.

Ms. Hashemi shared her vision and expectations for her role:

"I am looking forward to learning about the exciting research that scientists are conducting at Rockefeller University and help build connections with community networks, strengthening the institution's relationships with community members, service providers and advocates. I welcome this opportunity to work with researchers at Rockefeller University and help get them excited about community-engaged research. I am motivated to take on this role with a deep belief in the importance of rooting scientific research in community needs and priorities to improve community health and wellbeing."

Please welcome Ms. Hashemi to Rockefeller. She can be reached at [ahashemi@rockefeller.edu](mailto:ahashemi@rockefeller.edu) and 212-327-7373.

## Nayaab Khawar, MS, New Project Manager joins the Clinical Research Office

By Editorial Staff



Ms. Nayaab Khawar joined the Clinical Research Office at the Rockefeller University Hospital and Center for Clinical and Translational Research in the role of Project Manager of the Empowering the Participant Voice (EPV) project led by the P.I., Dr. Rhonda Kost, Director of the Clinical Research Support Office, and co-director of the Center's Community Engaged Research Core.

Under Dr. Kost's leadership, Rockefeller has been a national leader in rigorously assessing the experiences of individuals who participate in clinical research studies, with a goal of using those data to improve the clinical research enterprise and the satisfaction of those who volunteer to participate in studies. As part of this effort, the National Center for Accelerating Clinical Translational Science (NCATS) of the National Institutes of Health (NIH) granted Rockefeller University \$2.7 million to develop new infrastructure facilitating collection of research participant feedback for widespread adoption. Through collaboration across

six Clinical and Translational Science Award (CTSAs) hubs, the team will develop a consensus on the best way to configure a common infrastructure, and teams will locally engage institutional, community, and patient stakeholders for input on how to best reach different populations and how to make results valuable to different audiences. As the project manager for this grant, Ms. Khawar is responsible for planning the project timeline for execution of the aims, coordinating the collaboration between the six sites, working with the PI to coordinate the development of the technical implementation and manage it locally, conduct program evaluation, and disseminate the infrastructure across the C TSA hubs and the broader scientific community.

Dr. Kost and Ms. Khawar have already made great progress in the project timeline and deliverables. The [EPV](#) project website provides information about the project and collaborating sites, upcoming events, tools and resources, and access to the Research Participant Perception Survey that Dr. Kost has developed and validated in studies of more than 5,000 research participants.

Ms. Khawar received her Master of Science in epidemiology from Columbia University and a Bachelor of Arts from The New School. Prior to joining Rockefeller University, Ms. Khawar worked in clinical research management at various institutions, including New York-Presbyterian Brooklyn Methodist Hospital, the New York City Department of Health and Medical Hygiene, and the New York City Center for Travel and Tropical Medicine. Ms. Khawar's research has focused on pediatrics

and maternal health, and her studies have been published in peer-reviewed academic journals. She has presented her research at national and international conferences.

Ms. Khawar shared her vision and expectations for her role:

"I have worked for many years in clinical research and I understand from my experience that participants are an essential component of research and clinical trials. Dr. Kost has been one of the trailblazers in the field of translational science and the importance of the participants' experience and viewpoint, which led to the development of the Research Participant's Perception Survey, a validated tool used to collect participant feedback and the tool that we are using for the EPV project. Utilizing this survey as a shared tool will allow collaborators at other institutions to gain valuable feedback and improve research experiences for participants at their sites. Not only are we trying to improve the research experience, but we hope to help institutions to understand the perspectives of underrepresented populations and to disseminate the project broadly to create the evidence base for intra-institutional benchmarking and the sharing of best practices."

Please welcome Ms. Khawar to Rockefeller. She can be reached at [nkhawari@rockefeller.edu](mailto:nkhawari@rockefeller.edu) and 212-327-8408.

## The First Effective Therapy for Meningococcal Meningitis

By Elizabeth (Betsy) Hanson



Flexner, Simon

Courtesy of the Rockefeller Archive Center



Flexner's laboratory at the Founder's Hall, 1908.

Courtesy of the Rockefeller Archive Center

In the winter of 1904-1905 meningococcal meningitis swept through New York City, killing more than 3,000 people as part of a worldwide pandemic. Simon Flexner (1863-1946), director of the newly established Rockefeller Institute for Medical Research, was appointed to a city health department commission to investigate the epidemic.

A renowned pathologist, Flexner knew that a bacterium caused the meningitis since it had been identified in 1887 and could be cultured easily. In addition, an antiserum that could kill the bacterium was available, made from the blood of horses infected with the it, but the therapy was being administered by subcutaneous injection and was not effective. Flexner also was familiar with cerebrospinal meningitis, having been part of a team that identified it during an epidemic among Maryland coal miners in 1893. From 1904 to 1907, he brought this field experience and his laboratory skills to bear on the disease. Using cultures from New York victims of the disease, he inoculated guinea pigs and monkeys to study the course of infection and ways of administering antiserum. He recognized that the problem was getting the antiserum where it was needed, in the brain, and thus he delivered it into the fluid that bathes the spinal column and the brain by a spinal (intrathecal) injection. The first human subjects received intrathecal injections of antiserum during a 1907 epidemic in Ohio. The death rate from the disease—which had been 75 percent—was cut in half. It

remained the only effective therapy for three decades, until sulfa drugs and penicillin became available. The success of this treatment, which was widely reported in newspapers, impressed John D. Rockefeller, Sr. and helped persuade him to pledge funds, in 1908, to build the Rockefeller Hospital. By 1913, Flexner could report on the serum's effectiveness in treating 1300 patients around the world.

The therapy's success also depended on having a potent antiserum, which was difficult to make. For several years scientists at the Rockefeller Institute prepared and distributed thousands of bottles of antiserum a year, free of charge. During World War I, outbreaks of meningitis in army barracks in Europe created a new demand for the antiserum. Scientists in Flexner's laboratory both developed a more efficient way to prepare the antiserum and, with support from the Rockefeller Foundation, distributed it during the war.

Simon Flexner received a medical degree from the University of Louisville in 1889. The next year he began a fellowship under William Henry Welch at the Johns Hopkins University, and early in 1893, he visited university laboratories in Europe. When the Johns Hopkins Medical School opened in 1893 Flexner was appointed to the faculty in pathology. He moved to the University of Pennsylvania in 1899, as professor of pathology. In 1901

Flexner was appointed to the Board of Directors of the newly formed Rockefeller Institute for Medical Research. He became the Institute's first director in 1902, remaining there until his retirement in 1935. In 1937 and 1938 he served as Eastman Professor at Oxford University. Among many awards and honors Flexner was elected to the American College of Physicians (1895) and the U.S. National Academy of Sciences (1908). Flexner's position at Rockefeller allowed him to become a leader in scientific publishing, in communicating about science to the public, and in guiding the development of graduate and postgraduate science education in the United States and abroad. His scientific contributions include the identification of Flexner's bacillus, a species of *Shigella* that causes tropical dysentery. With his son, James Thomas Flexner, he wrote a biography of his mentor: *William Henry Welch and the Heroic Age of American Medicine* (1942, 1993). Simon Flexner was the brother of Abraham Flexner, author of the 1910 "Flexner Report"—the most important work in reforming medical education in the history of the U.S.—and founder and first director of the Institute for Advanced Studies in Princeton, NJ.