THE ROCKEFELLER UNIVERSITY HOSPITAL
CENTER FOR CLINICAL AND TRANSLATIONAL SCIENCE

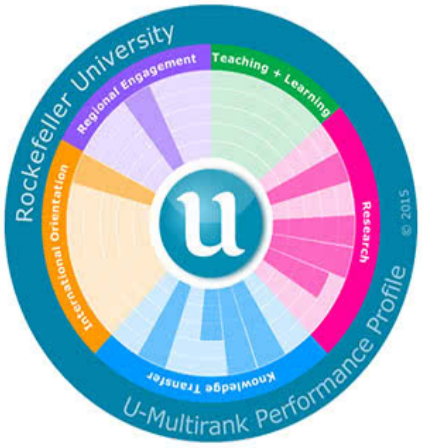
Spring 2017

Center for Clinical and Translational Science
e-NEWSLETTER

Center News

Rockefeller Tops Ranking of 1,300 Universities in Measures of Scientific Impact and Productivity

By Alexander MacWade



In an international comparison of universities, Rockefeller University ranked first place in categories related to scientific impact and research productivity. The results, which were released last month by the European Commission–funded organization U-Multirank survey, incorporate data on more than 1,300 institutions in over 90 countries.

For the third consecutive year, Rockefeller took the survey's top spot for scientific impact, based on the proportion of publications in the top 10 percent of those most frequently cited worldwide. The ranking, which placed Rockefeller above much larger institutions compares Rockefeller's publications to those of other institutions published in the same field and in the same year. When the data were adjusted to reflect institutional size, Rockefeller also ranked first in research productivity, both in terms of the overall number of publications per year, and the citation rate of its publications.

Rockefeller also came in first place for the second year in a row in a size-normalized ranking of the number of patents awarded, and it came in second place for the number of its publications cited in patents.

Established by the European Commission in 2014, U-Multirank compares international universities across five broad dimensions: teaching and learning, research, knowledge transfer, international orientation, and regional engagement. The data included in the rankings are drawn from a number of sources, including information supplied by international bibliometric and patent databases.

The Center for Clinical Translation Science 2017 External Advisory Board Meeting

By Editorial Staff

The Center for Clinical Translation Science (CCTS) External Advisory Board (EAB) Meeting was held on February 16, 2017. The EAB is led by Dr. Edward Benz, President and CEO, Dana Farber Cancer Institute, and is composed of Tesheia H. Johnson, MBA, MHS, Chief Operations Officer, Yale Center for Clinical Investigation, and Associate Director of Clinical Research for Yale School of Medicine; Margaret McCabe, PhD, RN, PNP, Director, Nursing Research, Medicine Patient Services at Boston Children's Hospital; Dr. Emma Anne Meagher, Vice Dean & Chief Clinical Research Officer at University of Pennsylvania Perelman School of Medicine; Dr. Lloyd Michener, Professor and Chairman, Duke Department of Community and Family Medicine and Director of Duke Center for Community Research; Rebecca Moen, MBA, Chief Administrative Officer at Duke Clinical & Translational Science Institute; Dr. Mark Alan Musen, Professor of Medicine (Medical Informatics) and of Biomedical Data Science and Director of Stanford Center for Biomedical Informatics and Research at Stanford University; Muredach P. Reilly, MB, MS, Director, Herbert and Florence Irving Professor for Medicine at Columbia University Irving Institute for Clinical and Translational Research; and Dr. Roger Vaughn, Vice Dean for Academic Advancement Professor, Department of Biostatistics at Columbia University.

During the morning session, the EAB members heard a presentation from Dr. Barry Coller, Director of the CCTS detailing the history of the Center, the current scientific and educational programs, and the plans for the future. The other leaders of the CCTS were present and answered questions from EAB members as they arose. The EAB then split into smaller working groups to focus on specific topics. During the working lunch, Dr. Manish Ponda and Dr. Louis Cohen, both graduates of the CCTS KL2 Clinical Scholars program, presented data from their research projects and described the role the Clinical Scholars Program played in their career development. The meeting closed with the EAB summarizing its findings, and making a number of extremely valuable suggestions to further strengthen the CCTS programs. The Senior Staff of the CCTS has already begun implementing the EAB's recommendations.

Overall, the EAB congratulated the CCTS on its "exemplary program" that "has impacted a broad community of clinical and translational scientists both locally and nationally." The committee identified key commendable features

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Dr. Gwenyth Wallen Delivers the 2017 Beatrice Renfield Lectureship in Research Nursing

By Rita Devine, RN, MPA

The Rockefeller University Hospital and the Heilbrunn Family Center for Research Nursing hosted the annual Beatrice Renfield Lecture in Research Nursing on March 7, 2017 in the Carson Family Auditorium. Dr. Barry Coller, Physician-in-Chief of the Rockefeller University Hospital began the event with a short tribute to Nancy Ellicott, Rockefeller University Hospital's first Superintendent of Nursing, who established the standards for the practice of clinical research nursing and invented several novel devices to improve nursing care. Dr. Patricia Eckardt, Director of the Heilbrunn Family Center for Research Nursing, hosted the program and introduced this year's speaker, Gwenyth Wallen, PhD., R.N.

Dr. Wallen's presentation, "Clinical Research Nursing and Nursing Science: A Perfect Partnership" focused on the specific objectives of the National Institutes of Health Clinical Center, as well as the distinct yet interdependent roles that nurse scientists and clinical research nurses play in advancing healthcare throughout the continuum from bench to bedside.

Dr. Wallen is the acting Chief Nurse Officer and Chief of Nursing Research and Translational Science for the NIH Clinical Center, a 200 bed research hospital that supports the clinical activities of the 27 NIH Institutes and Centers. Dr. Wallen directs all patient care units at the NIH Clinical Center, managing a staff of approximately 600 clinical research nurses and healthcare workers. As a member of the Center's

Gwenyth Wallen, PhD., R.N.

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A Community- Academic Partnership to Understand the Correlates of Successful Aging

By Kimberly S. Vasquez, MPH and Rhonda G. Kost, MD

RU-CCTS, Clinical Directors Network, and Carter Burden Network stakeholders at Metro East 99th St

RU-CCTS, Clinical Directors Network, and Carter Burden Network stakeholders at the 2017 Association for Clinical and Translational Science Conference

Food generally brings people together, and the new community-academic partnership between The Rockefeller University Center for Clinical and Translational Science (RU-CCTS), Clinical Directors Network (CDN), and Carter Burden Network (CBN) is no exception. Carter Burden Network is a non-profit multi-site senior community services organization on the Upper East Side of Manhattan and East Harlem that serves primarily low-income and vulnerable racial/ethnic minority seniors. In addition to a large day program at the 109th Street Leonard Covello Senior Center, it also serves individuals who were in long-term institutional settings before they moved into the beautiful and modern Metro East 99th Street facility.

RU-CCTS, CDN, and CBN share a common interest in understanding the correlates of successful aging in this population and in building a partnership and infrastructure to enable translational research to advance the health of seniors. RU-CCTS is committed to engaging populations across the life span, including hard-to-reach and underserved populations, such as low-income and minority seniors. To that end, the new RU/CDN/CBN partners are currently conducting a RU-CCTS-funded Pilot Project to characterize the health status and health challenges of the CBN population in preparation for future comparative effectiveness and mechanistic research studies.

The relationship between RU-CCTS and CBN started in October 2015 at the annual Lenox Hill Senior Health Fair organized by NYC Council member Ben Kallos, where the RU-CCTS bio-nutritionists Andrea Ronning and Glenis George-Alexander hosted a nutritional information table, and RU-CCTS Community Engagement Specialist, Ms. Kimberly Vasquez, discussed RU-CCTS's collaborative research goals with leaders from several senior services organizations, including CBN. Nutrition is an important issue for seniors, many of whom have health challenges, and often subsist on limited budgets that limit food choices. In fact, food insecurity is among the greatest concerns of CBN seniors. In March 2016, the bionutrition team proposed conducting outreach to senior groups to conduct cooking demonstrations of affordable, easy-to-prepare, nutrient-dense recipes. CBN leadership immediately expressed interest and in the ensuing months, Ms. Ronning and Ms. George-Alexander conducted

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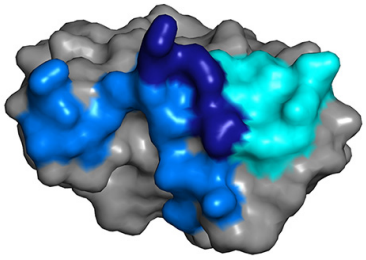
Discovery of a Zika antibody Offers Hope for A Vaccine

By Wynne Parry



Researchers have found natural antibodies that prevent Zika infection by latching onto a part of the virus. Credit: Jennifer R. Keeffe, Anthony P. West, Jr., and Pamela J. Bjorkman

A recent study from Dr. Michel Nussenzweig's and Dr. Charles Rice's laboratories found neutralizing antibodies to the Zika virus in blood samples from subjects in Mexico and Brazil. The antibodies appeared to have been initially generated in response to an earlier infection by a related virus that causes dengue.

"In the near future, these antibodies could be very useful. One could envision, for example, administering them to safely prevent Zika among pregnant women or others at risk of contracting the disease," says Davide F. Robbiani, a research associate professor in the Nussenzweig lab. He and Leonia Bozzacco, a research affiliate in Rice lab, led the study, which appeared in *Cell* in May.

The team's detailed examination of the interaction between this antibody and the virus also revealed a new potential strategy for developing a vaccine. A mosquito-borne virus, Zika usually causes mild symptoms in those who contract it. However, dramatic effects can appear in the next generation. Babies born to women infected during pregnancy are at risk of devastating neurodevelopmental abnormalities. The only way to prevent Zika is to avoid mosquito bites; there are currently no vaccines or other medical measures.

Through collaborators working in Pau da Lima, Brazil, and Santa Maria Mixtequilla, Mexico, they obtained blood samples from more than 400 people, collected shortly after Zika was circulating. Individual responses to the same pathogen can vary greatly. Yet a deeper analysis of samples from six of the volunteers with the most promising antibodies revealed a surprise: five of them contained nearly identical antibodies. When the team examined these closely related antibodies' performance against Zika, one, obtained from a Mexican volunteer's blood, stood out. When this antibody, called Z004, was given to mice rendered vulnerable to Zika, it protected them from developing serious infections.

An infection begins when the virus, traveling in a spherical particle studded with the viral envelope protein, latches onto a host cell and gains entry into the cell. Faced with a viral threat, the human immune system generates antibodies that recognize the virus and stop it from invading cells. The team set out to find antibodies tuned to a particular target: a part of Zikas envelope protein that the virus needs to infect cells.

To get a closer look at the interaction between the antibody and a fragment of the virus' envelope protein, scientists in Pamela J. Bjorkman's lab at Caltech determined the molecular structure formed as the two units interacted. The structure identified a ridge on the viral protein to which the antibody attaches. While some efforts to develop a vaccine use all or most of the virus to stimulate the immune system, the researchers believe it could be safer to employ only a tiny fragment containing this ridge.

Zika isn't the only virus with this ridge, as it is also present in the envelope proteins of other viruses in the same family. The dengue 1 virus, a close relative of Zika and one of four types of dengue, has a similar ridge and the Z004 antibody neutralized this virus as well.

A look back at samples from the Brazilians, collected six months before Zika arrived by a team led by Albert Ko of Yale University, revealed evidence of prior dengue 1 infections in some—and a potential explanation as to why certain people's immune systems fared better against Zika. "Even before Zika, their blood samples likely had antibodies that could interact with this same spot on the envelope protein," says Margaret R. MacDonald, a research associate professor in Rice's lab. "It appears that, much like a vaccine, dengue 1 can prime the immune system to respond to Zika."

Study Identifies "Night Owl" Gene Variant

By Wynne Parry

Illustration by Jasu Hu

Researchers in Dr. Michael Young's laboratory reported in *Cell* in April that a variant of the gene *CRY1* slows the internal biological clock—called the circadian clock—that normally dictates when you feel sleepy each night and when you're ready to wake. People with the "night owl" variant of this gene have a longer circadian cycle than most, making them stay awake later. Their 24 hour sleep-wake cycle is delayed, making them energetic long after most people have fallen asleep.

Going to bed late has its downsides however, since most people with DSPD are forced to wake up before their bodies tell them to in order to get to work or school on time, leading to fatigue during the day.

Dr. Young commented that, "Compared to other mutations that have been linked to sleep disorders in just single families worldwide, this is a fairly impactful genetic change." According to the new research, the mutation may be present in as many as one in 75 people in some populations.

Diagnosing night owls

The Centers for Disease Control and Prevention estimate that between 50 and 70 million adults in the US have a sleep or wakefulness disorder. These conditions—ranging from insomnia to narcolepsy—can predispose people to chronic diseases including diabetes, obesity, and depression.

People who self-categorize as night owls are often diagnosed with delayed sleep phase disorder (DSPD).

Free-running sleep cycles

Young's lab has studied the circadian clock for more than three decades, identifying a number of the genes involved in keeping flies, humans, and other animals on schedule when it comes to eating and sleeping.

To find out whether mutations in any known circadian genes were linked to DSPD, Young—along with research

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RUH Achieves Full Accreditation from The Joint Commission (TJC)

By Riva Gottesman, MPH

On November 9, 2016, two Joint Commission surveyors arrived at Rockefeller University Hospital for an unannounced 2-day survey. The Joint Commission (TJC) is an independent not for profit organization that accredits and certifies more than 21,000 health care organizations and programs in the US. TJC accreditation and certification is recognized nationwide as a symbol of quality that reflects an organization's commitment to meeting high performance standards. The standards focus on important patient organization functions that are essential to providing safe and high quality care. An organization undergoes an onsite survey every three years to maintain its accreditation.

TJC assigned two surveyors to conduct the accreditation evaluation, one a nurse and the other an engineer. The nurse meticulously examined medical records, interviewed the nursing staff, and thoroughly reviewed hospital policies. In addition, she reviewed the Medical Staff's credentialing process, competencies assessment, and Human Resources documentation. The engineer reviewed Life Safety and Environment of Care documentation and conducted a Life Safety tour of the hospital. After addressing all of the issues identified by the reviewers, Rockefeller University Hospital was awarded accreditation for another three years. This achievement reflects the entire staff's absolute commitment to patient safety and the highest quality medical care, as well as the commitment of the support departments that insure that the Hospital is structurally sound and has all systems needed to prevent and respond to events that challenge the safety of the Hospital environment.

Town Hall Meeting On "Living with Face Blindness"

By Christina Pressl, MD, Rhonda Kost, MD, and Kimberly S. Vasquez, MPH

On December 13th, 2016, more than 150 members of the public gathered in person and virtually to join the first town hall meeting on "Living with Face Blindness" hosted by The Rockefeller University. The meeting's primary intent was to bring patients, friends, families, doctors, communities, and all other stakeholders together for an evening filled with informative discussion and exchange about face blindness (also known as prosopagnosia).

The gathering was initiated by Dr. Christina Pressl, Clinical Scholar in Dr. Winrich Freiwald's Laboratory of Neural Systems. Dr. Pressl studies the neuronal underpinnings of face perception in the lab and also conducts clinical research studies involving individuals with face blindness. The program was designed to include both scientific and lay presentations, and to incorporate questions and feedback from patients and other participants.

Supported in part by a Pilot Award to Dr. Pressl from The Rockefeller University Center for Clinical and Translational Science (CCTS), the event was coordinated in close collaboration with the CCTS Community Engagement Core under the guidance of Drs. Rhonda Kost and Jonathan Tobin, the Community Engagement Specialist Kimberly S. Vasquez MPH, and the staff from Clinical Directors Network. Through a live CCTS-supported webcast, the event was accessible to a large virtual audience, including interested individuals from the U.S., Canada, Germany, Austria, and other countries. The webcast was later archived as part of an eLearning library accessed by clinicians from a broad variety of clinical settings. A link to this archive can be found below.

Dr. Freiwald took the audience on a lively and fascinating journey through the history of perception neuroscience up to current developments in the field of vision neuroscience, with an emphasis on face perception research. The next speaker was Dr. Duchaine, an associate professor in the Department of Psychological and Brain Sciences at Dartmouth College, Dr. Duchaine has worked with prosopagnosic individuals for many years at Harvard University. Together with Dr. Ken Nakayama, he developed today's most widely used test in research for the assessment of face perception abilities - the Cambridge Face Memory Test. This tool has helped many individuals who are troubled by day-to-day face recognition difficulties document their impairment. Dr. Duchaine provided detailed insights into various aspects of prosopagnosia research and the current state of knowledge on the condition. In one form termed developmental prosopagnosia, individuals experience face recognition difficulties from an early age. Another form, known as acquired prosopagnosia occurs when face perception difficulties arise after damage to certain areas of the brain.

Dr. Joe DeGutis, Ph.D., Investigator and Instructor at Harvard Medical School, and Co-director of the Boston Attention and Learning Laboratory, spoke about his studies to improve face recognition skills of face blind individuals.

Dr. Heather Sellers, author of *You Don't Look Like Anyone I Know*, and Professor of English Literature at the University of South Florida has shared her life-experience of face blindness through writing and public presentations. As the keynote speaker at the town hall meeting, Dr. Sellers spoke about her struggle to recognize people by their face, and her detective-like efforts to find the causes of her difficulty. Dr. Sellers vividly described the relief she felt when her face recognition challenges were diagnosed as face blindness. In fact, as it turned out, it was Dr. Duchaine who tested Dr. Seller's and confirmed her inability to recognize other people's faces. Dr. Sellers said that she hopes that by sharing her story, and through efforts like the town hall meeting, others will find out how to get tested, get the help they seek, and obtain answers to their questions. The evening ended with a panel discussion, during which questions from the on-site and the online audiences were addressed.

If you would like to find out more, please visit ***http://www.faceweb.me.*** The recorded, three-hour long webcast video and more information can be found via the ***websites' blog page*** or via the ***eLearning library***. Furthermore, more information about Dr. Pressl's currently ongoing clinical research studies can be found ***here.***

New CTSA Program Initiative: Trial Innovation Network

By Donna Brassil, MA, RN, CCRC

The Trial Innovation Network is a CTSA program that leverages the expertise, skills, and knowledge of the entire CTSA Consortium. It is composed of three key organizational partners – the CTSA Program Hubs, the Trial Innovation Centers (TICs), and the Recruitment Innovation Center (RIC). Each partner plays a unique and essential role.

The vision for the TIN is to creatively address critical roadblocks in clinical trial development and conduct, and thus accelerate the translation of novel interventions into life-saving therapies. The TIN focuses on operational innovation, operational excellence, and collaboration. It features a single IRB system, master contracting agreements, quality by design approaches, and evidence-based strategies to recruitment and patient engagement. The TIN will also be a national laboratory to study, understand, and innovate the process of conducting clinical trials.

The Rockefeller University Trial Innovation Network (TIN) Hub Liaison Team

At Rockefeller University, we have a TIN Hub Liaison Team. The goal of the team is to help investigators develop and implement clinical trials in the most efficient manner.

- Providing input/Navigation before protocols are submitted to the TIN.
- Recognizing the essential contributions and efforts of local teams in executing multi-center clinical trials.
- Creating a culture in which key stakeholders play unique and important roles, and help to build a national system to conduct clinical trials better, faster, and more cost-effectively.

The CTSA Program Hubs are the frontline of the TIN. They use their experience and knowledge of the local environment to innovatively operationalize the Network at their Institutions, tailoring general Network plans into more specific action plans best suited for their Hubs.

The Rockefeller University TIN Hub Liaison Team is comprised of Barry Coller, James Krueger, Barbara O'Sullivan, Rhonda Kost, Maija Neville-Williams, Teresa Solomon, Vanessa Smith, and Donna Brassil.

Trial Innovation Center (TIC) and Recruitment Innovation Center (RIC)

The TICs are located at Duke/Vanderbilt, University of Utah, and Johns Hopkins/Tufts. They are charged with streamlining the TIN's procedures.

There is one Recruitment Innovation Center (RIC) at Vanderbilt and it specializes in the development and consolidation of electronic methods for facilitating recruitment.

TRIAL INNOVATION NETWORK PROPOSAL PROCESS

Investigators can request consultations and services for multi-center clinical trials and studies from the TIN from a menu of choices. Some consultations may lead to further development into full clinical protocols that may be implemented in the TIN.

Services Offered

The TIN first offers an initial consultation or specific service depending on the funding status of the proposal. Investigators are invited to submit proposals to the TIN at any time.

F**or Studies that Already Have Funding or Have Already Applied for Funding:**

Trial Innovation Network Services: Service requests are prioritized based on resource availability. Specific services include Standard Agreement and Central IRB Operationalization, Recruitment Materials and a Recruitment Plan, a Community Engagement Studio, and an EHR -Based Cohort Assessment.

For Studies that are Still Under Development and Have Not Yet Been Funded:

Trial Innovation Network Initial Consultation

- An initial consultation may include, for example, study design, budget recommendations, a proposed timeline, recruitment assessment, and study feasibility assessment.

Trial Innovation Network Comprehensive Consultation

- Based on the outcome of an Initial Consultation, the next step may be a Comprehensive Consultation. A Comprehensive Consultation cannot be selected by an investigator, but is a decision that is reached by the TIN after the Initial Consultation and after approval by the Proposal Assessment Team and NCATS.
- A Comprehensive Consultation involves mutual agreement and commitment by the investigator and the TIC/RIC to collaboratively develop the proposal into a protocol. In addition, one of the goals in the Comprehensive Consultation process is to obtain input from the CTSA Hubs on the protocol. The estimated number of hours of consultation time for a Comprehensive Consultation has not yet been determined.
- A Comprehensive Consultation could include an array of enhanced consultations such as in-depth protocol development, statistics, recruitment feasibility, recruitment plans, study budgets, and other key elements.
- After a Comprehensive Consultation, an investigator prepares a clinical trial application for submission to an NIH Institute for funding or to an industry or philanthropic partner. The TICs and RIC would serve as the Coordinating Centers for the study and the CTSA Hubs would be potential sites.

For detailed information on the TIN process and guidelines, log onto the toolbox at h**ttps://trialinnovationnetwork.org/elements/trial-innovation-network-proposal-process/**

Prior to submitting a TIN Project Proposal, investigators must discuss the proposal with his/her CTSA Program Hub Principal Investigator and the TIN Liaison Team, so feel free to speak to any of us about your interest.

The Center for Clinical Translation Science 2017 External Advisory Board Meeting

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of the CCTS, including "the spectrum of subject recruitment initiatives, the incorporation of patients' preferences into protocol development, the Translational Navigation Program that supports the trainees as they design, plan and execute their research protocols, and efforts that engage scientists with their communities to accelerate translation." The committee also noted that CCTS has been very effective in actively disseminating its innovations – these included "the graduate tracking survey system; informed consent for next gen sequencing; and the approach to implementing a navigation service to PhD scientists to facilitate translation. The number of publications on the science of innovation is commendable."

Dr. Gwenyth Wallen Delivers the 2017 Beatrice Renfield Lectureship in Research Nursing

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executive team and a widely respected authority in nursing science, Dr. Wallen also plays a central role in setting national standards for patient care in the clinical setting, and for defining how nursing research can be integrated into the biomedical research infrastructure.

In her presentation, Dr. Wallen described the process by which nurse-led research projects are proposed, evaluated, funded, and conducted at the NIH Clinical Center. She provided several examples of successful projects in which the data obtained were immediately put to excellent use in enhancing patient care and clinical research quality.

The lecture was attended by 103 guests, including 24 representatives from the Rockefeller University Hospital nursing department, the Clinical Research Office, and the Facilitation Office, as well as several representatives from Rockefeller Laboratories. Also in attendance were the current and past presidents of the International Association of Clinical Research Nurses. 73 guests registered to view Dr. Wallen's presentation via a webcast provided through the Clinical Director's Network (CDN). The webcast is available through the CDN website under the CCTS Webcast Series section.

Drs. Barry Coller, Gwenyth Wallen, and Patricia Eckardt

Seminars in Clinical Research upcoming 2017 dates

September 6, 2017
September 13, 2017
September 27, 2017
October 4, 2017
October 11, 2017
October 25, 2017
November 1, 2017
November 8, 2017
November 15, 2017
November 29, 2017
December 6, 2017
December 13, 2017

A Community- Academic Partnership to Understand the Correlates of Successful Aging

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a series of cooking demonstrations at CBN's Metro East 99th Street Social Adult Day Program. They focused on recipes geared to the foods distributed by CBN from the Common Pantry.

In July and August 2016, CBN leaders Mr. Bill Dionne, Executive Director of CBN, and Dr. Dozene Guishard, Director of Metro East 99th Street Social Adult Day Program, attended the monthly meeting of the RU-CCTS Action Committee for Community Engaged Research (ACCER) to discuss interest and priorities, and in August, the ACCER members – RU-CCTS Community Engagement Core Co-Directors Drs. Rhonda G. Kost and Jonathan N. Tobin (President/CEO Clinical Directors Network), the bionutrition team, and Dr. Barry Coller, Maija Neville-Williams, MPH, and Kimberly Vasquez, MPH, visited the CBN Center and the Metro East 99th Street Social Adult Day Program. They learned that the most pressing concerns for senior residents – as identified through surveys and use of services – in addition to food insecurity are depression, social isolation, and falls. CBN leadership has created many programs to address these concerns and needs.

Employing the Community-Engaged Research Navigation (CEnR-Nav) model to incorporate and align shared interests, strengths, and requirements, the RU/CDN/CBN partners developed a join research proposal and competed successfully for a 2016-2017 RU-CCTS Community-Engaged Research Pilot Award. The study is designed to: 1) Engage the Carter Burden residents, day participants, staff, and leadership in developing a sustainable community-academic partnership, 2) Use descriptive epidemiology to characterize the health status of CBN seniors, focusing on measures of frailty, including contributions from chronic conditions, as well as cardio-metabolic, musculoskeletal, psychosocial and nutritional factors, 3) Create a database for data acquisition at CBN sites to collect and integrate service utilization and research data, and 4) Develop robust longitudinal measures of frailty and related problems that can be used to assess the impact of different interventions to improve the health of the community.

The partnership is making progress across all of the aims. In 2016-2017, the team conducted a series of engagement meetings with more than 40 CBN residents to ascertain their main concerns related to healthy aging and make sure the study-related assessments will capture these priorities. Enrollment of 240 participants is actively underway to provide the baseline measurements for future studies.

In April 2017, Dr. Guishard of CBN joined several RU/CDN team members to co-present a poster at the 2017 Association for Clinical Translational Science Meeting in Washington, D.C. At the same meeting, Drs. Kost and Tobin presented an invited talk on the CEnR-Nav model of engaging community stakeholders into early translational research, emphasizing the investigators' perspectives through videos of RU scientists who conduct mechanistic/CEnR projects. This shined a spotlight on the importance of community-academic partnership in the design and conduct of research projects that reflect community priorities and that are designed to accelerate translation of new scientific knowledge into improved population health.

Study Identifies "Night Owl" GeneVariant

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associate Alina Patke, the first and co-corresponding author of the new paper—collaborated with sleep researchers at Weill Cornell Medical College. Subjects were asked to spend two weeks in a laboratory apartment that was isolated from all cues to the time of day, eating and sleeping whenever they were inclined. Researchers also collected skin cells from each person.

Most people will follow a roughly 24 hour sleep-wake cycle when put in such a free-run environment. However, a DSPD subject that caught the researcher's interest not only stayed up late, but had a cycle that was about 30 minutes longer. Moreover, changes in body temperature and hormones that cycle along with the circadian clock—including melatonin, which helps regulate sleep—were also delayed. "Melatonin levels start to rise around 9 or 10 at night in most people," says Young. "In this DSPD patient that doesn't happen until 2 or 3 in the morning."

When the researchers examined the DNA from the DSPD patient, one variant stood out; a mutation in *CRY1*, a gene that had already been implicated in the circadian cycle.

In a healthy circadian clock, several genes turn on and off during a 24 hour cycle. The protein made by *CRY1* is normally responsible for suppressing some of these genes during certain parts of the cycle. But Young and Patke discovered that the mutation identified in the patient made the C*RY1* protein more active than usual, keeping other clock genes switched off for a longer period of time.

The researchers reached out to other members of the patient's family and discovered five relatives who shared the mutation in *CRY1*. All of them had signs of DSPD.

With a collaborator in Turkey, Dr. Young's group first identified many unrelated families and dozens of Turkish people with the *CRY1* mutation. After contacting them and administering interviews and questionnaires, the researchers were able to confirm that 38 people with the mutation had altered sleep behavior, while none of their relatives without the *CRY1* mutation had unusual sleep patterns.

Finally, after scouring larger genetic databases for *CRY1* mutations, Young's group calculated that as many as one in 75 people of non-Finnish European descent have at least one copy of the DSPD mutation. The mutation is dominant, which means that having just one copy of it can cause a sleep disorder.

The researchers say that right now there's no established benefit for DSPD patients in being tested for the *CRY1* mutation.

"Just finding the cause doesn't immediately fix the problem," says Patke. "But it's not inconceivable that one might develop drugs in the future based on this mechanism."

For now, many DSPD patients are able to control their sleep cycles—and get to bed earlier than their body wants—by following strict schedules.

Some patients seem to be helped by getting strong light exposure during the day.

The team already has future studies planned to work out whether *CRY1* mutations also affect the metabolic cycles of people with DSPD, since the human circadian cycle is known to not only regulate sleep, but also hunger and levels of metabolites and hormones.

Meet the Scholar: Christina Pressl, M.D.

By Michelle Romanick

Christina Pressl

Dr. Christina Pressl joined the Clinical Scholars Program at the Rockefeller University in 2014. Dr. Pressl received her M.D. from the Medical University of Graz in Austria, and she joined Dr. Winrich Freiwald's Laboratory of Neural Systems as an Instructor in Clinical Investigation after completing three years of radiology residency at the Medical University of Vienna.

As a child, Dr. Pressl developed a fascination for nature, spending many hours in her parent's garden inspecting insects and local plant life. She followed this passion with intensive biology classes in high school and her interest in medicine developed from spending time in her father's private practice. After graduating from high school, Dr. Pressl traveled for cultural experience, learning new languages, as well as auditing university classes in diverse fields of studies, all related to the natural sciences. She went on to attend the Medical University of Graz and participated in a number of research programs during her studies and throughout radiology residency, which fostered her interest in neuroradiology and neuroscience.

During residency, Dr. Pressl did a research sabbatical at Memorial Sloan Kettering Cancer Center under the mentorship of Dr. Mark Dunphy, and working with a group of outstanding doctors and scientists utilizing radiopharmaceuticals for the diagnosis, evaluation, and treatment of cancer. It was during this time she learned about the research in Dr. Freiwald's Laboratory on neural mechanisms of face perception. This led her to apply to the Clinical Scholars Program with Dr. Freiwald as her mentor, and she started the program in July 2014.

Dr. Pressl's research focuses on studying the neuronal machinery of face perception by applying advanced imaging techniques and batteries of behavioral tests. In her main project she is working with Temporal Lobe Epilepsy (TLE) patients to understand how the face perception network is affected by ongoing epileptic seizures and to investigate what impact temporal lobe surgical resection has on the system. In other projects, the focus lies on the developmental form of face blindness, including the search for genetic contributions. Dr. Pressl is active in outreach endeavors, developing a website, www.faceweb.me, organizing a town hall meeting for patients with face blindness in December in conjunction with the Community Engagement and Recruitment Cores as well as Clinical Directors Network (CDN). She is also collaborating with the New York City-Clinical Data Respository Network (NYC-CDRN) and Dr. Jonathan Tobin to query a large number of electronic health records to learn more about the prevalence and medical impact of face blindness.

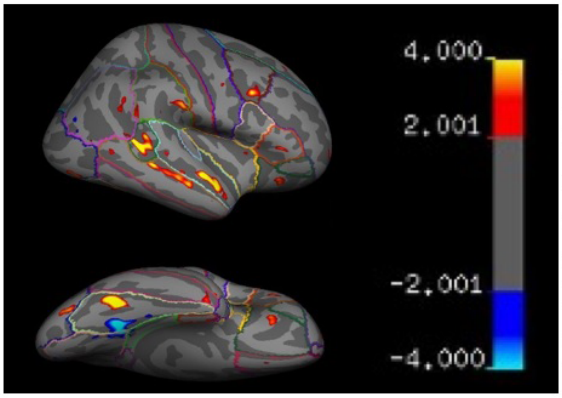
When asked about her experience as a Scholar and Chief Scholar, Dr. Pressl replied, *"I experienced many priceless teaching moments in the program. The Clinical Scholars program has shaped me as physician scientist and a team leader. I have autonomy to develop and lead my research, and I have been encouraged to create a team to drive the research. I also have the freedom to ask questions and test theories. The spirit among the Scholars, as well as throughout the Rockefeller University, has encouraged me to actively seek the exchange of ideas.*

The Clinical Scholars are very diverse in their disciplines and scientific backgrounds and this diversity generates robust discussions on a wide variety of stimulating topics. Curiosity connects us and drives us, and diversity is the key to developing a flourishing, motivated, and successful community. Often it is the views of people outside my own field, who look at the science from a different angle, that helps me see aspects of my own work that I had not recognized before. This intellectual input and stimulation perpetually sparks new ideas, leads to new approaches, and ultimately fosters development."

Dr. Pressl was accepted into the David Rockefeller Graduate Program, and will pursue her PhD degree by extending her research in the Freiwald Laboratory of Neural Systems.

Two example stimuli used to assess individuals' ability to recognize faces.

fMRI Analysis



Warm colored areas are more active when faces are presented compared to category blocks when objects are presented

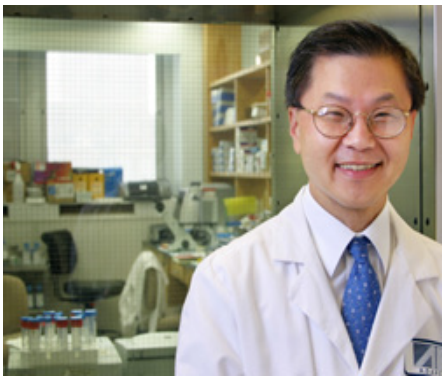
Rockefeller Historical Vignette: Combination Antiretroviral Therapy: The Turning Point in the AIDS Pandemic

By Elizabeth (Betsy) Hanson

In 1981 hospital wards in the United States and elsewhere began filling with patients who had unusual infections that developed because their immune systems had become very weak. Their underlying disease soon had a name—acquired immunodeficiency syndrome (AIDS)—and within a few years scientists discovered the virus that caused it, HIV-1. But until the mid-1990s an AIDS diagnosis was a death sentence. Then, David Ho (1952 -) and colleagues at the Rockefeller-affiliated Aaron Diamond AIDS Research Center discovered that treating patients with a combination of three or more antiretroviral drugs could keep the virus in check. The initial clinical trials of this therapy were carried out with patients at the Rockefeller Hospital. Today, in the developed world, AIDS is a manageable chronic disease thanks to the "AIDS cocktail" of combination antiretroviral therapy.

Ho arrived at this approach to AIDS therapy after studying what the virus does in the body of an infected person. Fastidious quantitative studies with patients at the Rockefeller University Hospital revealed that HIV-1 replicates continuously at an astonishingly fast pace. Over time, the immune system becomes depleted and cannot protect people infected with HIV-1 from everyday pathogens in the environment that don't usually lead to problems. These studies of viral dynamics changed the conceptual paradigm for understanding HIV-1 infection and led to the new therapeutic strategies. They also found that HIV-1 does a sloppy job of copying its genetic material as it reproduces. Within the body of a single infected person, many different mutated versions of the virus exist. HIV-1 can change quickly, and so it quickly evolves resistance when an infected person takes a single drug. But Ho and coworkers found a way to corner the virus: by giving patients three or four drugs at a time, HIV-1 could not mutate rapidly enough to evade all of them. By 1996 they had succeeded in reducing HIV-1 levels to the point of being undetectable in a group of patients treated with the new therapy.

Many drugs targeting different steps in the HIV-1 replication cycle are available. Yet antiretroviral medications control

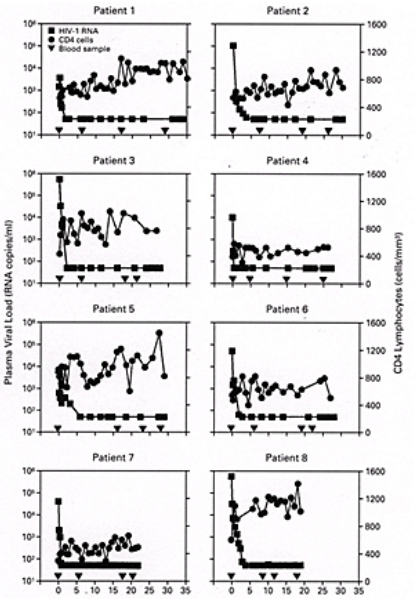


David Ho

HIV-1 infection rather than eradicate it, and are not accessible to the vast majority of the 33 million people worldwide who are infected. Since 2001 Ho has turned to the development of novel AIDS vaccines, with work both in the laboratory and with human subjects at Rockefeller University Hospital and abroad. He heads a consortium of scientists in this pursuit, supported by the Bill and Melinda Gates Foundation Collaboration for AIDS Vaccine Discovery. Ho's research group also is investigating the use of monoclonal antibodies to prevent and treat HIV-1 infection.

David D. Ho received his undergraduate degree from the California Institute of Technology (1974) and his MD from Harvard Medical School (1978). He completed his residency in internal medicine at the University of California, Los Angeles (UCLA), School of Medicine (1982), and then completed a fellowship in infectious diseases at Massachusetts General Hospital and Harvard Medical School (1985). He has held academic appointments at Harvard Medical School, the UCLA School of Medicine and the New York University School of Medicine. Ho has been scientific director and chief executive officer of the Aaron Diamond AIDS Research Center since 1990 and was named professor and physician at Rockefeller in 1996. He is the Irene Diamond Professor at Rockefeller.

Among many honors, Ho has received the Edward Ahrens Award in Clinical Investigation and the Friendship Award from the State Council of the People's Republic of China in 2003 and was awarded the Presidential Citizens Medal in 2001. He received the Hoechst Marion Roussel Award (now the Aventis Award) in 1999, the Squibb Award from the Infectious Diseases Society of America in 1996, the New York City Mayor's Award for Excellence in Science and Technology in 1993 and the Ernst Jung Prize for Medicine in 1991. He was a scientific honoree of the New York Academy of Medicine in 1998 and Time magazine's Man of the Year in 1996. He is also the recipient of 12 honorary doctorates. Ho is a member of the American Academy of Arts and Sciences, the National Academy of Medicine, and the Academia Sinica, as well as a foreign member of the Chinese Academy of Engineering.



Antiretroviral therapy in the eight patients with HIV. From N Engl J Med, 1999, 340: 1605-1613