Program Project Grants at the National Institute on Aging support multiple teams of researchers, who closely collaborate using complementary approaches to clarify a fundamental aspect of Alzheimer’s Disease (AD) or related disorders that holds special promise for understanding its causes and developing novel therapies.

The CDR Program Project, which is in its 17th year, has pioneered discoveries that have linked the genes causing AD to prominent defects appearing at the earliest stages of AD and potentially represent the most promising new targets for novel therapies to prevent or treat AD. In all forms of AD, the first biological abnormalities to appear
in the brain are related to a pathway by which neurons internalize life-sustaining materials from outside the cell within “endosomes”, deliver these building blocks to the proper destinations in the neuron, and recycle the surplus in “lysosomes” that metabolize unwanted cell materials, which could become potentially toxic. This material includes the hallmarks of AD pathology, β-amyloid peptide and tau protein, which accumulate in the AD brain along with massive amounts of undigested “waste” that collectively contribute to the degeneration of synapses and neurons leading to memory loss. The CDR team has provided evidence that the early failure of the “endosome-lysosome pathway” is fundamental to both normal synaptic functioning and memory as well as to the development of amyloid and tau-related “plaques and tangles”, which are the targets of drugs currently being tested in AD clinical trials with equivocal success so far. The Program’s overall premise is that defining the molecular basis for the defects in the endosome-lysosome pathway – given their early appearance and diverse cellular roles including ones in protein recycling, synapse regulation, and intracellular signaling – leads to novel therapeutic targets that broadly address AD at its biological origin and therefore hold considerable promise for drug development.

The Program, directed by Dr. Ralph Nixon, is titled **Cell and Molecular Pathobiology of Alzheimer’s Disease**, and consists of four research projects and three Core support elements. It addresses a major aspect of the “endosome-lysosome” pathway failure at the molecular level and at a translational level expected to identify specific drug intervention points and validate the efficacy of certain drugs or related approaches in disease models. **Project 1**, led by Dr. Paul Mathews addresses endosomes while **Project 3**, led by Dr. Efrat Levy, addresses the roles of endosomes in releasing neuroprotective or disease-related endosomal cargoes within smaller membrane bound compartments called exosomes. **Project 2**, led by Dr. Ralph Nixon, investigates the progressive failure of lysosomes to eliminate disease-related proteins and the therapeutic reversal of this failure, which has been shown to have diverse ameliorative effects in AD models. **Project 4**, led by Dr. Stephen Ginsberg, uses genomic analyses of single populations of neurons in AD brain to investigate the competence of cellular delivery routes to lysosomes (autophagy and endosomal) and molecular strategies to increase the efficiency of these critical clearance mechanisms. The discovery by CDR scientists of this striking failure of cellular clearance in AD brains has stimulated research world-wide, revealing promising new targets for drug development to slow or prevent AD.

In addition to the Program Project grants, Dr. Helen Scharfman of the CDR has received two recent R01 grants. The first is titled **Hilar Mossy Cells and Dentate Gyrus Function**. This goal of this project is to clarify how a unique cell type in the dentate gyrus called a hilar mossy cell contributes to the function of this part of the brain, which is involved in normal cognition and behavior. The dentate gyrus and hilar mossy cells have received increasing attention as more evidence has shown that the dentate gyrus is involved in many types of behavior, and appears to sustain loss of mossy cells in many neurological and psychiatric disorders.

Dr. Scharfman’s second grant is titled **Hyperexcitability in Alzheimer’s Disease**. This grant addresses the hypothesis that early in Alzheimer's disease there is overactivity in some parts of the brain and this contributes to the subsequent decline in brain function. The grant uses animal models that simulate different characteristics of humans with Alzheimer's disease, and uses these models to test new treatments to prevent or delay the onset of Alzheimer's disease.
“A Man of So Many Communities”

At the NAMI Rockland Awards Dinner, Outpatient Research Department Director Russell Tobe, MD, received the Florence Gould Gross Award to Friends of People with Mental Illness. The award was presented by RPC’s Liz Falco, MS, RN, who is also a NAMI Rockland Board Member. In her remarks, Liz shared some of the ways in which Dr. Tobe had been described to her by his NKI colleagues. Here are just a few:

“He is a well-rounded, great person!”
“Down to earth, kind, generous, loving, supportive”
“Truly a wonderful person to work with”
“Brings out the best in people”
“Great resource for our community”
“Bright, well trained and has a wealth of knowledge in child psychiatry”
“A man of the community”

Congratulations to Dr. Tobe for this well-deserved recognition!

Newly Minted

Kathy Peng, PhD, (Center for Dementia Research) successfully defended her doctoral thesis in August, and has received a fellowship to begin her post-doctoral work in the laboratories of Paul Mathews and Efrat Levy. Kathy received her BA in Behavioral Biology from Johns Hopkins. Her PhD, from NYU, is in Neuroscience and Molecular Pharmacology.

GRANTS RECEIVED

Drs. Efrat Levy (Dementia Research) and Mariko Saito (Neurochemistry) have received a five-year R01 grant entitled “Brain exosomes mediate cocaine-induced addiction” from the National Institute on Drug Abuse. Drs. Mitsuo Saito and Henry Sershen (Neurochemistry) are co-investigators. The goals of this project are to characterize the involvement of brain exosomes in cocaine-induced addiction. The study will identify the mechanisms behind the release of exosomes during cocaine administration and how exosomal content of proteins, lipids, and RNAs change during the course of acute and repeated cocaine administration followed by withdrawal. This study will identify new targets for addiction therapy as well as new biomarkers for cocaine addiction and withdrawal.
FROM AROUND THE INSTITUTE

CDR Hosts Senator Carlucci

On September 12, New York State Senator David Carlucci visited NKI and toured the Center for Dementia Research. The CDR’s recent funding success (see p.1) was announced on this occasion. Senator Carlucci’s past appropriation of State funds for a state-of-the-art microscope helped NKI’s scientists to secure the highly competitive federal grants.

Dr. Paul Mathews gives a demonstration for Senator Carlucci while Dr. Stephen Ginsberg looks on.

New Beginnings

After nearly 20 years at NKI, Janet Rosdil retired from her position as executive administrative assistant to Dr. Ralph Nixon in the Center for Dementia Research to pursue well-earned new adventures. Janet was the first person hired when the Nixon Laboratories for Molecular Neuroscience relocated from Boston to establish the CDR in 1998. Her recruitment from a position at New York Medical College was an auspicious beginning for the CDR, which saw rapid growth in size and international reputation in the Alzheimer’s Disease community. Janet’s contributions have been an essential component to the CDR’s continued success over two decades. Says Dr. Nixon, “Janet’s extraordinary dedication, professionalism, and interpersonal skills have earned her the deep respect and appreciation of the entire NKI community. Notably, she has also admirably represented the CDR well beyond NKI, frequently receiving accolades from colleagues at NYU and visiting scientists worldwide for her exceptional communication and organizational skills.” Janet will apply her many talents to new pursuits that will undoubtedly include more time with her family and grandchildren, and travel with friends and family. A gathering of nearly 60 NKI staff and alumni expressed their fond appreciation for Janet’s many kindnesses in a farewell reception outside of the new lab building on a beautiful sunny day, appropriately auspicious for the new chapters in her life.

CDR Director Ralph Nixon with Janet Rosdil, his long-time administrator
Certificates of Confidentiality

Certificates of Confidentiality (CoC’s) protect the privacy of subjects by limiting the disclosure of identifiable, sensitive information. As a rule, researchers never disclose identifying information about subjects who participate in research without the subject’s consent. However, there are situations where a subpoena from a court could require that a subject’s records be made available. CoC’s exist to protect subjects from this possibility. A CoC allows research subjects to participate in studies that require information about sensitive issues such as illegal drug use or criminal activity.

Researchers can obtain a CoC only if a determination is made that the research is of a sensitive nature and the protection is necessary to reach the research objective. The Office for Human Research Protections (OHRP) finds research to be “sensitive” if it includes any of the following: 1) information regarding sexual practices or preferences; 2) information regarding the use of alcohol, illegal drugs, or other addictive products; 3) Information concerning illegal behavior; 4) Information that can be destructive to the subject’s financial standing, employability, or reputation within the community, or that might lead to social disgrace or prejudice; 5) Information regarding the subject’s psychological state or mental health; 6) genetic information or tissue samples.

The CoC is only valid for a distinct period of time and indefinitely protects the information collected during the covered period. The requirements of a CoC apply to the investigator and all collaborators. A CoC must be obtained for each study and is nontransferable. When a CoC is used in a study, subjects should be informed and should also be made aware of the exceptions from protection. One such exception is that investigators may voluntarily disclose issues related to child abuse, suicidal ideation, and threats to others. Subjects are informed of the conditions of the CoC in a consent form.

On September 7, 2017, the National Institutes of Health (NIH) issued a notice of updates for CoC’s. Under this policy, CoC’s will become a condition of NIH grant awards and are issued as part of the grant process. The effective date of the policy is October 1, 2017, but it will apply retroactively to all NIH research that was initiated or ongoing on or after December 13, 2016, that falls within the scope of the policy. CoC’s will continue to be available through other Department of Health and Human Services agencies (such as the Centers for Disease Control and Prevention, and the Food and Drug Administration). Researchers should apply to the agency involved in the funding or regulation of the study. If a study is not supported by NIH funding, applications for CoC’s may be directed to the NIH via the normal existing application process.

**PUBLICATIONS OF NOTE**

**JAMA Psychiatry**

C-BIN Director Michael Milham, MD, PhD is a coauthor of this paper on white matter abnormalities in childhood disorders appearing online in *JAMA Psychiatry*.


The publication was announced in this NYU Langone Health press release.
Vilma Gabbay, MD (Clinical Research) is the lead author of this open access paper appearing in Translational Psychiatry.


Elizabeth Phelps, PhD (Emotional Brain Institute) published this research on the effect of stress on memory in PNAS.


Stephen Ginsberg, PhD (Dementia Research) is the corresponding author of this article now online in Hippocampus. Melissa Alldred, Shaoli Che, and Irina Elarova of NKI are among the other contributors.


Xavier Castellanos, MD (Clinical Research) coauthored this editorial appearing in the September issue of The American Journal of Psychiatry.

Castellanos FX, Elmaghrabi SE. On the Road to Physiological Models of Brain Function in ADHD. Am J Psychiatry. 2017 Sep 1;174(9):825-826.

Members of Dr. Daniel Javitt’s Schizophrenia Research Program have a new publication appearing in Neuropsychopharmacology. Contributors to the paper are Migyung Lee, Andrea Balla, Henry Sershen, Pejman Sehatpour, and Peter Lakatos.


This article by Helen-Maria Lekas, PhD (Social Solutions and Services) and her Columbia University colleagues appears online in the journal AIDS and Behavior.

Members of the LeDoux Lab, including Lorenzo Díaz-Mataix and Robert Sears with the Emotional Brain Institute at NKI, published this open access paper in Learning & Memory.


Three recent articles by NKI authors appear in the open access journal Scientific Reports from Nature Publishing. Elizabeth Phelps (Emotional Brain Institute) is the senior author of two of these, and Marcin Leszczynski (Translational Neuroscience Laboratories) is first author of the third.


In recent years, there has been a proliferation of citation performance metrics – tools and algorithms intended to help assess the relative performance of a journal, author, or article (think of the Journal Impact Factor, or the h-index). This blog post at The Scholarly Kitchen, Citation Performance Indicators - A Very Short Introduction, provides a nice summary of the main indicators currently in use.

A new publication from The Centers for Medicare & Medicaid Services and SAMHSA, A Roadmap to Behavioral Health: A Guide to Using Mental Health and Substance Use Disorder Services, is designed to serve as a behavioral health resource for consumers and offers important information about mental health and substance use disorder services, including definitions of behavioral health terms and guidance on how to find a behavioral health services provider, receive treatment, and obtain follow-up care.

Citing Medicine is the NLM style guide for authors, editors, and publishers. It provides assistance to authors in compiling lists of references for their publications, to editors in revising such lists, to publishers in setting reference standards for their authors and editors, and to librarians and others in formatting bibliographic citations. The guide is continually updated to keep pace with the rapidly changing nature of new format types, such as datasets available on the Internet.
More on Predatory Publishing

The problem of predatory publishing is not going away any time soon, and researchers should be alert to the danger. There is a new commercial product that tracks fraudulent journals, replacing the now-defunct “Beall’s List”. You can read a good review on The Scholarly Kitchen blog.

In addition, several recent articles (see below) address different aspects of the issue and provide some perspective. The Comment in Nature (1) sheds light on the scope and insidiousness of the problem. And the paper and letters by Manca et al. look at the effect in the neurosciences and neurology (3), the need for education and increased awareness (4), and the way in which unscrupulous journals can make their way into PubMed (2).


For more on journal inclusion in PubMed, and how it has changed over the years, see “A Confusion of Journals – What is PubMed Now?”, another blog on The Scholarly Kitchen.

DEPARTMENT OF WONDER

👍

FaceBook has faced waves of criticism recently, for selling ads that a Russian company used to influence the U.S. Presidential election, and more recently for allowing advertisers to target users based on racist language and hate speech. Has FaceBook’s technology run amok? That is the possibility considered in this New York Times article: Facebook’s Frankenstein Moment.

TIME

With guidance from curators, historians, and photo editors from around the world, Time magazine has assembled a group of photographs under the heading “The Most Influential Images of All Time”. Each selected photo is accompanied by a short essay, and some also include a brief documentary film. Without a doubt, these pictures are worth a LOT of words.

The NKI librarian is always available to assist with literature searching, citation searching (Web of Science, Scopus), bibliographic reference management, and the like. When you have any information needs, or questions about available resources, don’t hesitate to turn to us.

The library offers a comfortable, quiet space for reading, work, and small meetings. To use the library’s Wi-Fi network, ask the library staff for the password.

You can link to the NKI Library’s website from myNKI. The Library site includes quick links to the NYU Health Sciences Library and to the New York State Library, as well as links to NKI’s own library resources (journal finder, online catalog, PsychiatryOnline, etc.). Remote access is available using NKI’s VPN.
Monika Pawlik, PhD (Dementia Research) recently gave a seminar at the Universidad Nacional Autónoma de México, Department of Physiology, in Mexico City. She spoke about recent research on Alzheimer’s disease at the Center for Dementia Research.

**UPCOMING EVENTS AND SEMINARS**

**Social Solutions & Services Research Department Presents**

Jung Yeon Lee, PhD  
NYU School of Medicine  
Department of Psychiatry  

*Triple comorbid trajectories of alcohol use, tobacco use, and depressive symptoms as predictors of cannabis use disorders among urban adults*  
Tuesday, October 10th, 10:00 am

**NKI Presents**

Ipe Ninan, PhD  
NYU School of Medicine  
Department of Psychiatry  

*Novel Mechanisms in the Regulation of Aversive Behaviors*  
Tuesday, October 24th, 11:00 am  
Hosted by Donald Goff, MD

**Center for Dementia Research Seminar Series**

*Held on Thursdays at 10 am*

**Ottavio Arancio, MD, PhD**  
Columbia University  
*Rearranging the puzzle: an alternative view on Alzheimer’s disease*  
October 12th

**Tsuneya Ikeya, MD, PhD**  
Boston University School of Medicine  
*Recent progress in microglia and exosome mediated progression of Alzheimer’s disease*  
October 19th

**Shawn Ferguson, PhD**  
Yale School of Medicine  
*Lysosome function, dysfunction, and neurodegenerative disease*  
November 16th

**Keith Vossel, MD**  
University of Minnesota  
*Epileptic activity in Alzheimer’s disease: causes and clinical relevance*  
November 30th
Center for Biomedical Imaging and Neuromodulation Science Series

Held on Mondays at 11 am

Babak Ardekani, PhD
C-BIN at NKI
Department of Psychiatry, NYU

A New Algorithm for Automatic, Unbiased, Fast and Reliable Alignment of Longitudinal Structural MRI with Submillimeter Accuracy: Application to Aging and Alzheimer’s Disease Research

October 16th

Muhammad Parvaz, PhD
Department of Psychiatry, Icahn School of Medicine at Mount Sinai

Title TBA

November 20th

Heath Pardoe, PhD
Department of Neurology, NYU

Title TBA

November 27th

2017 International Mental Health Research Symposium

Hear the 2017 Outstanding Achievement Prizewinners and select Young Investigators present updates on leading research discoveries across brain and behavior disorders, and a special Keynote Presentation.

Friday, October 27th
9:00 am – 4:30 pm
Kaufman Music Center
129 West 67th Street, New York, NY 10023

Click here for more information.

Statewide Grand Rounds

Modern Practice of ECT for OMH Patients

Presenter: Joan Prudic, MD
Clinical Professor of Psychiatry, Columbia University Medical Center
Director of ECT at NYSPI and NY Presbyterian Hospital, CUMC

Panelist: Stuart Taylor, MD
Director of ECT and Associate Clinical Director for Medical Education, Creedmoor PC
Associate Clinical Professor of Psychiatry, Columbia University College of Physicians & Surgeons

Moderator: Jay Carruthers, MD
Medical Director, Bureau of Psychiatric Services
New York State Office of Mental Health

Wednesday, October 18th
1:00 – 2:30 pm
Broadcast in the Director’s conference room

4th Annual New York Metro Imaging Research Symposium

Hosted by the Quantitative Neuroimaging Laboratory in the Cognitive Neuroscience Division Columbia University

Thursday, November 30th
9:00 am – 4:00 pm

Click here for more information.
The Bureau of Psychiatric Services, in conjunction with the Bureau of Education & Workforce Development (BEWD), announced the availability of select Statewide Grand Rounds (SWGR) in the Statewide Learning Management System (SLMS), located at https://nyslearn.ny.gov/. CE credits are available upon successful completion of a course.

To access the SWGR, log in to the Statewide Learning Management System (SLMS), and click on Find Learning. Enter the course code or course name in the find box. After you have found the course you are looking for, click on the Enroll button and Launch the course.

For a list of available courses, contact bewd@omh.ny.gov.

Below is a list of references that have been added to the NKI publications database since the previous update. The full database contains over 5,600 items dating back to 1995, and can be searched from the myNKI website.


Castellanos FX, Elmaghrabi SE. On the Road to Physiological Models of Brain Function in ADHD. Am J Psychiatry. 2017 Sep 1;174(9):825-826.


