LEVY LAB INVESTIGATES THE ROLE OF EXTRACELLULAR VESICLES IN AGING AND NEURODEGENERATION

Contributed by Efrat Levy, PhD, and Pasquale D’Acunzo, PhD

For over ten years, Dr. Efrat Levy and members of her laboratory in the Center for Dementia Research have been studying vesicular transport as it relates to neurodegenerative disorders such as Alzheimer’s disease. In particular, they have been investigating the role of extracellular vesicles (EVs) and over time they have developed increasingly powerful methods of isolating and analyzing these minute particles. Papers published in 2012 (Pérez-González et al., 2012) and in 2017 (Pérez-González et al., 2017) described a novel method to isolate EVs from the interstitial fluid of the brain. The lab has used this method for the analyses of brain EVs during aging (Kim et al., 2022), in patients with neurodegenerative diseases such as Alzheimer’s disease (Pérez-González*, Kim* et al., 2020), in individuals with Down syndrome (Gauthier*, Pérez-González et al., 2017; D’Acunzo et al., 2019; D’Acunzo et al., 2021), in murine models of spinocerebellar ataxia (Zhang et al., 2021) and chronic cocaine exposure (Barreto*, D’Acunzo* et al., 2022), and in subjects carrying the apolipoprotein E4 allele, the greatest genetic risk factor for Alzheimer’s disease (Peng et al., 2019).

[* denotes equal contribution]
EVs are heterogeneous and encompass vesicles with different intracellular origins, functions, and molecular markers. Therefore, the Levy lab continuously worked to improve the original protocol to better fractionate known and novel brain EVs. The latest milestone on their journey is a recent publication in *Nature Protocols* (D’Acunzo et al., 2022) which details a high-resolution fractionation technique that better separates subpopulations of the known extracellular vesicles, the plasma membrane derived microvesicles and the late endosome-derived exosomes. Most importantly, the improved protocol revealed the existence of a different, previously unidentified type of EV that derives from mitochondria and that the authors named mitovesicles. The *Nature Protocols* article is accompanied by an online “Behind the Paper” feature authored by Dr. Pasquale D’Acunzo.

Dr. Levy’s laboratory is currently studying the pathways involved in mitovesicle exocytosis and the effects of their internalization, investigating the physiological and pathogenic roles of mitovesicles in the brain. The discovery of mitovesicles paves the way to study novel mechanisms that are relevant for neurodegenerative diseases and that likely have a contributive role in the development of dementia. Accordingly, mitovesicle research may suggest in the future novel and unexplored therapeutic directions and be useful to identify new diagnostic/prognostic markers in the blood.

**GRANTS RECEIVED**

**NIH**

Drs. Kerstin Pahl and Crystal Fuller Lewis (Social Solutions & Services) received an R01 from the National Institute on Aging for a project titled “*Structural Adversity and Life-Course Social Determinants of Stress Regulation and Epigenetic Aging in Midlife Adults.*”

**NIH**

Dr. Brian Russ (Translational Neuroscience Laboratories) received an S10 equipment grant from the National Institute of Mental Health titled “*Transcranial focused ultrasound platform for noninvasive neuromodulation.*”

**NIH**

Drs. Charles Schroeder, Sam Neymotin, and Stephan Bickel (Translational Neuroscience Laboratories) received an R01 titled “*Dynamic circuit motifs underlying multimodal interactions in primate auditory cortex*” from the National Institute on Deafness and Other Communication Disorders.

**NIH**

Drs. Crystal Lewis, Helen-Maria Lekas, and Babak Tofighi (Social Solutions & Services) have received an R34 from the National Institute on Drug Abuse titled “*Feasibility of pharmacy-delivered patient navigation + virtual buprenorphine + HIV services.*”

**NIH**

Dr. Ayana Jordan (Social Solutions & Services) received an R01 titled “Culturally-Responsive Integrated Harm Reduction Services for Black and Latinx People Who Use Drugs,” also from the National Institute on Drug Abuse.
Megan Gautier successfully defended her PhD thesis on September 2nd. Megan’s thesis advisor was Dr. Stephen Ginsberg (Dementia Research). Her research topic was “Impact of Maternal Choline Supplementation on Endosomal Pathology and Septohippocampal Circuit Vulnerability in a Mouse Model of Down Syndrome and Alzheimer’s Disease.”

On September 22nd, Dr. Abel Lajtha celebrated his 100th birthday! One of the founders of the field of neurochemistry, Dr. Lajtha became Director of the Research Institute for Neurochemistry and Drug Addiction at Wards Island in 1963. This later became the Center for Neurochemistry at NKI, which Dr. Lajtha has directed for decades.

Over his remarkably long and productive career, Dr. Lajtha has held numerous leadership roles and received many honors and recognitions. He was President of the Research Foundation for Mental Hygiene, Inc. from 1977 to 2018. He was also the Founder and longtime Editor-in-Chief of the journal Neurochemical Research and Founding Editor-in-Chief of the Handbook of Neurochemistry (now in its third edition). He was President of the International Society of Neurochemistry (1975-77) and the American Society for Neurochemistry (1979-81). In addition, he was elected member of the Slovenian Academy of Sciences, the Hungarian Academy of Sciences, the Indian Academy of Neuroscience, and the Armenian National Academy of Sciences.

Dr. Henry Sershen, a decades-long colleague whose career was nurtured by Dr. Lajtha, notes that “Abel was always one to help support others ... He is a remarkable person and scientist; and beyond science, he was an avid skier and tennis player – still playing tennis well into his 90s!”

To mark this occasion at NKI, the Neurochemistry entrance at will be named in Dr. Lajtha’s honor.
The FDA’s approval of Auvelity, an extended-release tablet that combines dextromethorphan and bupropion for the treatment of major depressive disorder in adults, was reported in this Psychiatric News Alert from the American Psychiatric Association. NKI’s Director of Clinical Research, Dr. Dan Iosifescu, is the senior author of two recent papers reporting the clinical trial results. This news was also reported in Psychiatric Times.

The NKI Community Building Committee’s Sweet September BBQ 2022 was a big success!

The laboratory of Salvador Dura-Bernal (Biomedical Imaging & Neuromodulation at NKI and SUNY Downstate) was recently featured in the NIH Director’s Blog (“The Amazing Brain: Where Thoughts Trigger Body Movement”). As noted in the blog, “In the Dura-Bernal lab, scientists develop software and highly detailed computational models of neural circuits to better understand how they give rise to different brain functions and behavior.”
Paul O’Connor and Dana Lam recently retired from their positions at NKI. We wish Paul and Dana all the best as they begin the next chapters of their lives!

Paul O’Connor was 15 years into an enjoyable career at Pan Am Airways (he played on the company basketball team all around the world!). But after Pan Am ceased operations in 1991, Paul soon found himself at NKI, where he worked in the Information Sciences Division until his retirement last month. Paul sent this note to his NKI colleagues:

It’s frightening to realize that 30 years have passed since I came to NKI. Among the memories I’ll cherish, moving into the new state-of-the-art building in 1998 was certainly a highlight. More than that, I’m a lucky guy to have made so many friends here, and most of all I’ve been impressed by the marvelous group of dedicated researchers and scientists I’ve encountered. Happy trails to all of you!

Dana Lam recently retired from her position in the OMH Clinical Laboratory. The following tribute is from her colleague Shaona Fang.

Dana Lam worked in the OMH Clinical Laboratory for about 14 years. She is well loved not only by her colleagues in the clinical laboratory but also by the personnel of the NY State psychiatric facilities, who she directly interacted with during her daily work. Dana is knowledgeable and competent in her assigned duties and beyond. It became a habit that we often went to Dana to resolve issues because problems are always solved beautifully with her help. In addition to her excellent services in our laboratory, Dana demonstrated her professional skills by solving problems over the phone with psychiatric facilities, patiently and friendly, which earned her the recognition of top-ranking employee during a customer satisfaction survey.

It was wonderful working with Dana. She promoted a positive culture in our laboratory and was admired by her colleagues. People around her are influenced by her warm, caring, friendly and diligent character. As a close friend of Dana, I feel comfortable and happy with her. Dana always brings me special dishes when she has a chance to go to Chinatown in NYC – such as chicken feet, duck wings, and other dry food that are not easy to get around our area. My family always enjoys her Moon Cakes for Moon festivals. Her fresh-picked bitter melon with shrimp is my favorite meal. Many thanks to Dana and I wish her a happy and healthy retirement!
**PUBLICATIONS OF NOTE**

**nature protocols**

Efrat Levy and members of her lab and the Center for Dementia Research Pasquale D’Acunzo, Yohan Kim, Jonathan Ungania, Rocio Perez-Gonzalez, Chris Goulbourne recently published this powerful new technique for isolating a variety of extracellular vesicles from brain tissue in *Nature Protocols*. The article is accompanied by an online “Behind the Paper” feature. To read more about this research, see page 1 above.


**Neuron**

Helen Scharfman (Center for Dementia Research) is the senior author of this paper in *Neuron* with lab members John LaFrancois and Swati Jain, and other coauthors.


**eNeuro**

Samuel Neymotin and numerous NKI colleagues in the Center for Biomedical Imaging & Neuromodulation published their latest research in the Society of Neuroscience open access journal eNeuro.


**Autophagy**

Ralph Nixon, Director of the Center for Dementia Research, and colleagues in his laboratory have two new articles in the journal *Autophagy*. The first of these is a short piece highlighting the *Nature Neuroscience* paper recently published by Ju-Hyun Lee et al.


Mala (Venkat) Rao is the corresponding author of this new research paper.

Sharifa Williams, Kerstin Pahl, Crystal Fuller Lewis, and Daniele Martino (Social Solutions & Services; Center for Research on Cultural and Structural Equity in Behavioral Health) recently published this new research in the Journal of Community Health.


Kerstin Pahl, Helen-Maria Lekas, Navin Sanichar, Sharifa Williams, and Gilbert Nick (Social Solutions & Services) are coauthors of this recent article in the Journal of Racial and Ethnic Health Disparities.


Brian Russ (Biomedical Imaging & Neuromodulation) coauthored this open access article appearing in PNAS.


Director of Clinical Research Dan Iosifescu is the first author of this clinical trial report in the Journal of Clinical Psychiatry. NKI coauthors are Umit Tural, Katherine Collins, and Erin McDonald.


Dr. Iosifescu is the senior author of another recent paper on photobiomodulation, this one appearing in the open access journal Photonics. This research was highlighted in a post by the Brain & Behavior Research Foundation (BBRF), from which Dr. Iosifescu received funding earlier in his career.

Nunzio Pomara (Geriatric Psychiatry) and NKI colleagues Chelsea Reichert Plaska and Ricardo Osorio coauthored this open access paper published in *Translational Psychiatry*.


Robert Smith, Henry Sershen, Abel Lajtha, and Matthew Grieco are NKI coauthors of this article recently published in *Frontiers in Psychiatry*.


Lila Davachi (Clinical Research) is the corresponding author of this recent paper in the *Journal of Neuroscience*.


Christopher Cain (Emotional Brain Institute) coauthored this open access paper appearing in *Learning & Memory*.

Ostroff LE, Cain CK. **Persistent up-regulation of polyribosomes at synapses during long-term memory, reconsolidation, and extinction of associative memory.** Learn Mem. 2022 Jul 26;29(8):192-202. PMID: 35882501.

Panos Roussos (Dementia Research) is a corresponding author of this article published recently in *Nature Genetics*.


Karl-Heinz Nenning (Biomedical Imaging & Neuromodulation) coauthored this open access article in *Die Radiologie*.

These free upcoming webinars from the Network of the National Library of Medicine may be of interest.

On October 20th, you can learn tips for self-promotion, self-marketing, and self-branding for advancing your career in “Science-Self-Fandom: How to promote your science and your worth”.

“How PubMed Works” is a series of four 90-minute classes on the following topics:
3. How PubMed Works: MeSH (Medical Subject Headings)

The first class is on November 2nd. Click the links for more information and to register for any of these webinars.

The Health, United States program, which brings together many sources of federal and external data, has launched a redesigned website which makes it easier to find and use accurate and reliable trend data on a variety of topics.

The Health, United States report is transitioning to an interactive, user-friendly product with web content. The updated product includes a redesigned topic-based website as well as the traditional report (forthcoming), now called the Annual Perspective. The new user-friendly website includes the data finder to access trend tables, a revamped structure, and a new look. The topic pages bring together key findings, featured figures, and new trend analyses.

PubChem is an open chemistry database at the NIH and is the world's largest collection of freely accessible chemical information.

Starting in December 2022, PubChem will serve as the National Library of Medicine's single source for chemical information. NLM is retiring ChemIDplus and the Drug Information Portal, two other chemical property information sites. All of the data found in ChemIDplus and the Drug Information Portal is currently available and will continue to be available in PubChem.

For more information about using PubChem, see About PubChem.

“Would You Like to Live to a ‘Ripe Old Age?’” A former editor of JAMA has some advice for doing so. But perhaps Dr. Lajtha (see p. 3) could also teach us a thing or two in that department.

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, etc.).
**EVENTS AND SEMINARS**

**NKI Virtual Town Hall Meeting**

*2022 Virtual Town Hall Meeting and Employee Recognition Event*

will be held on Tuesday, December 13th at 11 am

**Center for Biomedical Imaging and Neuromodulation Science Series**

Held on Mondays at 11 am via Zoom

https://childmind.zoom.us/j/2142826575?pwd=dXISedRCAw9RNWRpZ2R5Y0dPQkw4UT09

**Theresa Desrochers, PhD**
Brown University
October 31st

**Wenhao Zhang, PhD**
UT Southwestern
November 7th

**Center for Dementia Research Neuroscience Seminar Series**

Held on Thursdays in the NKI conference room

**Frederick Maxfield, PhD**
Weill Cornell Medical College
*Interaction of microglia with amyloid plaques*
November 10th

**D. Allan Butterfield, PhD**
University of Kentucky
*Amyloid beta-peptide, brain lipid peroxidation and Alzheimer disease: Focus on the intersection of HNE-bound proteins, glucose dysmetabolism, altered proteostasis network, and neuronal death*
December 15th

**Statewide Grand Rounds**

**COVID-19 & Schizophrenia: Updates on a Systemic Immune Challenge**

**Presenter**

Katlyn Nemani, MD
Clinical Research Psychiatrist, NKI
Research Assistant Professor, Department of Psychiatry, NYU Grossman School of Medicine

**Moderator**

Jay Carruthers, MD
Medical Director, Bureau of Psychiatric Services, NYS OMH

Wednesday, October 19th
1:00 – 2:15 pm

The New York State Office of Mental Health (OMH) regularly hosts an interactive video broadcast covering the latest research, technology, and treatment implementation in the fields of psychiatry and psychology. These programs are recorded, and the archived Statewide Grand Rounds programs can be viewed on the OMH website.
2022 International Mental Health Research Symposium (Virtual & In-Person)

The Brain & Behavior Research Foundation (BBRF)’s annual research symposium will be held on Friday, October 28th. Join to watch presentations on leading research discoveries across brain and behavior disorders by the Foundation’s 2022 Outstanding Achievement Prizewinners.

For more information and to register, go to:
https://www.bbrfoundation.org/event/international-mental-health-research-symposium

On the Shoulders of Giants Scientific Symposium

The On the Shoulders of Giants Scientific Symposium is the Child Mind Institute’s annual celebration of scientific achievement in child and adolescent psychiatry, psychology, and developmental neuroscience. This year’s symposium will explore the impact of gender on brain development and mental health disorders with talks by pioneering neuroscientist Margaret McCarthy, PhD, and her proteges. The presentation will be followed by an expert roundtable.

For more information and to register, go to:

NKI ON THE ROAD

Department of Psychiatry Grand Rounds

Ayana Jordan, MD, PhD (Social Solutions & Services) presented the NYU Department of Psychiatry Grand Rounds on September 22nd. Dr. Jordan’s topic was “Cultural Considerations for Addiction Research: Looking to the Past to Inform the Future”.

Dr. Balapal S. Basavarajappa (Dementia Research) served as Chair and was a presenter in the Brain Sciences 2022 World Mental Health Day Webinar held on October 10th. The topic of his talk was “CDK5 in the Pathogenesis of FASD-like Phenotypes”.

NKI PUBLICATIONS UPDATE

Below is a list of references that have been added to the NKI publications database since the previous update. The full database contains over 7,000 items dating back to 1995 and can be searched from the myNKI website.


Stevenson TJ, Peng KY, Rouse ML Jr, Alward BA, Ball GF. Social regulation of immediate early gene induction in gonadotropin releasing-hormone 1 neurons and singing behavior in canaries (Serinus canaria). Physiol Behav. 2022 Sep 8;113959. PMID: 36088981.


