

Herbert & Jacqueline Krieger Klein Symposium on Alzheimer's Disease and Neurodegeneration

April 3, 2018

Organized by the Rutgers Brain Health Institute

Alumni Lecture Hall, B-552, MSB, Rutgers-New Jersey Medical School, Newark, NJ

8.00 – 8.30 AM Registration, Breakfast and Welcome

Gary Aston-Jones, PhD

Director, Brain Health Institute

8.30 – 8.45 AM *Murray and Charlotte Strongwater Endowed Chair in Neuroscience and Brain Health*

Chancellor Brian Strom, MD, MPH

Rutgers Biomedical and Health Sciences

8.45 - 9.00 AM **Andrew Thomas, PhD**

Senior Associate Dean, GSBS, Thomas P. Infusino Endowed Chair, Professor and Chair of Pharmacology, Physiology and Neuroscience, RBHS-NJMS.

Dean Robert Johnson, MD, FAAP

Sharon and Joseph L. Muscarelle Endowed Dean, Professor of Pediatrics, RBHS-NJMS

9.00 – 9.15 AM **Hon. Herbert C. Klein, Esq.**

Rutgers alum, emeritus member of the Rutgers Foundation Board of Overseers, Represented NJ in US Congress, served in NJ General Assembly

9.20 – 10.00 AM **Endowed Chair Lecture: Luciano D'Adamio, MD, PhD**

Professor of Pharmacology, Physiology and Neuroscience, RBHS-NJMS.

Herbert & Jacqueline Krieger Klein Endowed Chair in Alzheimer's Disease and Neurodegeneration Research

“Studying AD and Dementia Pathogenesis in Knock-in Animals”

10.05 – 10.35 AM **Qian Cai, MD, PhD**

Assistant Professor of Cell Biology and Neuroscience, Rutgers-New Brunswick

“Axonal Transport and Autophagy-Lysosomal Regulation in Alzheimer's Disease”

10.35 – 10.50 AM Refreshment Break

Steven Levison, PhD

Professor of Pharmacology, Physiology and Neuroscience, Director, Laboratory For Regenerative Neurobiology, RBHS-NJMS

10.50 – 11.20 AM

“How Insights from Alzheimer’s Disease Research Inform the Mechanisms of Tertiary Neurodegeneration After a Perinatal Brain Injury”

Wilma Friedman, PhD

Professor of Cellular Neurobiology, Rutgers-Newark

11.25 – 11.55 AM

“The p75 Neurotrophin Receptor Promotes Neurodegeneration After Brain Injury”

Keynote: Jie Shen, PhD

Professor, Director, Udall Center of Excellence for Parkinson's Disease, Brigham and Women's Hospital, Harvard Medical School.

12.00 – 1.00 PM

“Lessons from Genetic Studies of Alzheimer’s Disease”

1.15 – 2.30 PM

Lunch

Laszlo Zaborszky, MD, PhD, DSc

Distinguished Professor, CMBN, Rutgers-Newark

2.35 – 3.05 PM

“The Cholinergic Basal Forebrain in MCI and Alzheimer’s Disease”

Maral Mouradian, MD

William Dow Lovett Professor of Neurology and Director of the Center for Neurodegenerative and Neuroimmunologic Diseases, RBHS-RWJMS

3.10 – 3.40 PM

“Novel Disease Modifying Therapeutic Strategies in Parkinson’s Disease”

Chery Dreyfus, PhD

Professor and Chair Department of Neuroscience and Cell Biology, RBHS-RWJMS

3.45 – 4.15 PM

“Enhancing Recovery from a Demyelinating Lesion through the Actions of BDNF: The role of Astrocytes and Metabotropic Glutamate Receptor Agonists”

Teresa Wood, PhD

Professor of Pharmacology, Physiology and Neuroscience, Rena Warshow Endowed Chair in Multiple Sclerosis

4.20 – 4.50 PM

“White Matter Vulnerability: Intracellular Signaling Pathways in Oligodendroglia that Regulate Demyelination and Repair”

Hon. Hebert C. Klein and Jacqueline Krieger Klein



The symposium is being held to honor the establishment of the Herbert C. and Jacqueline Krieger Klein Endowed Chair in Alzheimer's disease and Neurodegeneration at Rutgers Brain Health Institute. The Endowed Chair was established by Hon. Hebert Klein and, his late wife, Jacqueline Krieger Klein.

Mr. Klein obtained a BA in Political Science from Rutgers College in 1951 and went on to obtain his JD and LLM degrees from Harvard and New York University, respectively. Mr. Klein was a member of the New Jersey General Assembly from 1972 to 1976, where he was chair of the majority caucus. He wrote the law that created the New Jersey Economic Development Authority and was co-counsel on bond issue for New Jersey Sports and Exposition Authority. In 1993, Mr. Klein was elected to the 103rd Congress. During his tenure in the United States House of Representatives, Mr. Klein was a leader on the House Banking Committee, where he was responsible for several major legislative initiatives. He co-authored the bills that authorized interstate branch banking and was the architect of the provision which sparked passage of the legislation that ended the problems in the savings and loan industry. Mr. Klein also served on the House Science Committee, where he co-authored the National Competitiveness Act which helped American industry regain global control in manufacturing. He was a member of Governor James Florio's transition team, and a Trustee of the Democratic National Committee. He joined Genova Burns in September 2015 as Of Counsel and member of the Commercial Real Estate and Redevelopment Law Practice Group. Prior to joining Genova Burns, he was a Partner with the firm Nowell-Amoroso-Klein-Bierman. In addition to his law practice, Mr. Klein serves as a Trustee at First Real Estate Investment Trust of New Jersey, an equity real estate investment trust.

Mr. Klein is an Emeritus member of the Board of Overseers at Rutgers Foundation and former member of Rutgers Board of Trustees. He served on the Class of 1951's 65th Reunion Campaign Committee and previously served as the Campaign Co-chair for his class' 60th reunion. As a Rutgers student, he was editor-in-chief of the Targum, a member of the Crown and Scroll and Cap and Skull honor societies, as well as a brother of Tau Delta Phi. He is a Loyal Son of Rutgers. Mr. Klein and his late wife, Jacqueline, have been generous donors to Rutgers. He is a member of the Society of Queen's College, which recognizes donors whose lifetime giving to Rutgers has exceeded \$1 million.

Mrs. Jacqueline Krieger Klein, who passed away in April 2017, was a graduate of Wellesley College, where she established the Jacqueline Krieger Klein '53 Fellowship. Jacqueline was a member of the Democratic National Committee, a member of the Board of Trustees of the New Jersey Y Camps, a member of the Board of Trustees and former Secretary of the Boys & Girls Club of Clifton as well as a member of the Board of Trustees of the Jewish Federation of Passaic and Clifton. Mr. and Mrs. Klein were married for 64 years.

Rutgers Alzheimer's Disease Research Center (RuADRC)

Alzheimer's disease (AD) and related dementias are a major cause of disability and death in the elderly. Approximately 6 million people have been diagnosed with AD and related dementias and the aging of America's population suggests that the number of Alzheimer's patients in the US will, by 2050, increase to nearly 14 million people. Worldwide, approximately 40 million people have AD and related dementias. This number could also climb to nearly 120 million by 2050. With Americans spending \$226 billion annually to treat the symptoms of AD, and other dementias, rather than the cause of this disease itself, this disease alone could cost Americans \$1.1 trillion by 2050. As 5% of AD cases are familial and ~95% are sporadic, disease-modifying drugs that treat both sporadic and familial AD are desirable. Despite recent advances in our understanding of basic biological mechanisms underlying AD and related dementias, we do not yet know how to prevent AD and related dementias, nor do we have an approved disease-modifying intervention. A major reason that these problems persist is that current animal models of AD and related dementias have not been able to predict the effectiveness of proposed therapies, so that many that have moved into clinical trials fail, which greatly slows the development of new therapies and increases their cost. Thus, there is a great need to develop the next generation of animal models (NexGeMo) of AD and related dementias to provide greater predictive power of potential therapies and thus accelerate the drug testing/clinical trial pipeline.

Vision

The ultimate goals of the proposed RuADRC are:

- To develop therapies to cure AD and related dementias or, at the very least, effectively slow down the course of disease progression.
- To discover novel diagnostic and prognostic biomarkers that can forewarn the initiation of pathogenic processes before symptoms occur and also be used to monitor disease progression and treatment efficacy.

To achieve the above goals, research at RuADRC will focus on identifying disease mechanisms using genetic, cellular, organismal and behavioral approaches in animal and human model systems. Understanding of disease mechanisms will help uncover pathways that need to be targeted by drugs to achieve therapeutic efficacy. Development of relevant *in vitro* and *in vivo* models will be important for pre-clinical evaluation of novel drugs. A dementia clinic for patient recruitment, assessment and treatment will also be needed for translating research to clinic.

To fulfill the vision, RuADRC will have three components:

Component 1: Include cores for- development of novel animal models; histopathology; small animal imaging; electrophysiology; and, behavioral testing.

Component 2: Include cores for- developing novel human cell model systems, such as isogenic hiPSC lines carrying AD genetic variants; high-throughput drug-screening; and immunohistochemistry.

Component 3- Include a Dementia clinic and cores for- development of novel neurocognitive psychological tests and new neuro-cognitive rehabilitation approaches; human pathology assessment, human imaging; and collecting human samples (brain tissue, cerebrospinal fluids, blood/serum samples etc.).

Mr. Klein, has recently donated, generously, additional funds to support the recruitment of a junior faculty to help fulfill the above vision of growing RuADRC into a premier AD research Center.

Hebert C. and Jacqueline Krieger Klein Endowed Chair in Alzheimer's Disease and Neurodegeneration Research



Luciano D'Adamio, MD, PhD

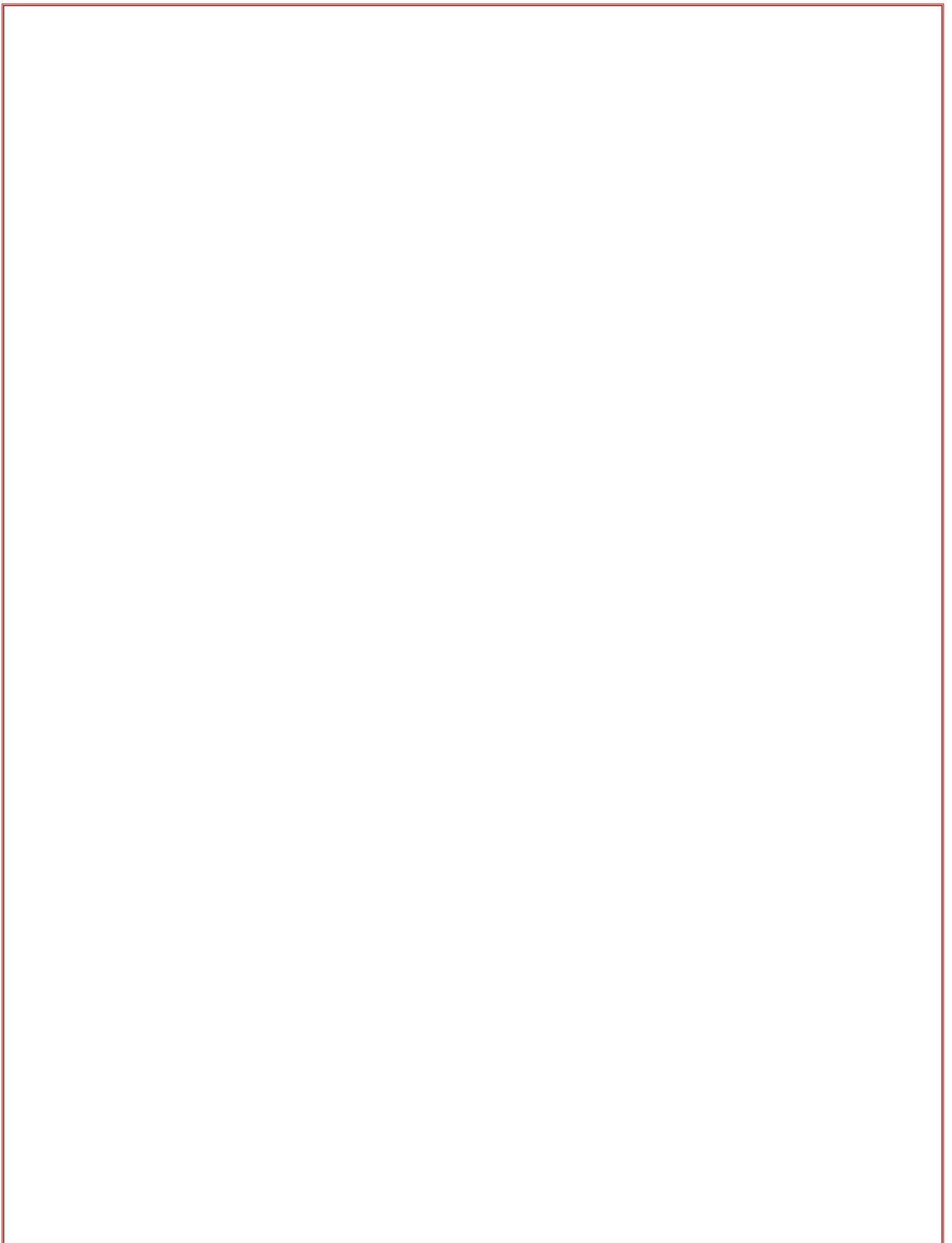
Dr. Luciano D'Adamio, MD, PhD, Professor of Pharmacology, Physiology and Neuroscience and Professor of Neurology at the New Jersey Medical School will hold the Herbert C. and Jacqueline Krieger Klein Endowed Chair in Alzheimer's disease and Neurodegeneration Research. Dr. D'Adamio is also the Associate Director of the Rutgers Brain Health Institute for Alzheimer's disease and Neurodegeneration Research focus area.

Dr. D'Adamio, obtained his MD from the University of Perugia, Italy. Working on his thesis project at the Dana Farber Cancer Institute, Harvard Medical School, he obtained his PhD from Sapienza University of Rome, Italy. In 1996, as an intramural principal investigator at the National Institutes of Health, his lab was the first to identify the role of cell death pathways in Alzheimer's disease, starting his interest in neurodegeneration. In 2000, he joined the Department of Microbiology and Immunology, Albert Einstein College of Medicine, Yeshiva University as an Associate Professor and was promoted to Professor with tenure in 2004. He was recruited to Rutgers from Albert Einstein College of Medicine in June 2017.

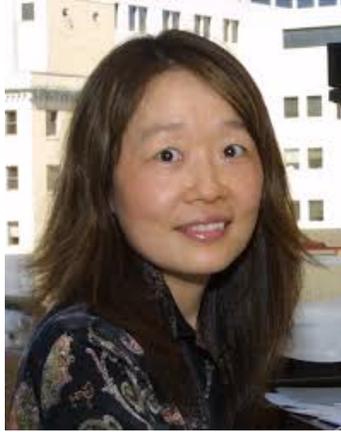
Dr. D'Adamio is one of the world's leading expert in the field of Alzheimer's disease research. During the last 15 years, his lab has used genetic approaches to dissect the mechanisms of age-related neurodegeneration occurring in Alzheimer disease, Familial British dementia and Danish dementia. He has published more than 97 peer-reviewed articles in high impact journals such as *Science*, *Cell*, *Neuron*, *PNAS* etc. His papers have been cited more than 7500 times with an H-index of 46. His contribution to the field of Alzheimer's disease has been recognized by the 2001 Alzheimer Award from the Journal of Alzheimer's Disease and the 2011 Zenith Award from Alzheimer's Association. He has also received numerous awards from the Alzheimer's Association, the Irene Diamond Foundation, Edward N. and Della L. Thome Memorial Foundation.

Dr. D'Adamio research has been continuously funded by the National Institutes of Health and other funding agencies since 2000. He is currently the Principal Investigator on multiple grant awards from the National Institute of Aging at NIH. He holds five patents on his discoveries and is the scientific co-founder of three companies- RemeGenix, Inc, Kappa Life Sciences and SienaGen, s.r.l.

Dr. D'Adamio is a member of the editorial board of *Current Alzheimer Research* and *Molecular Neurodegeneration*, both of which are major journals in the field of Alzheimer's disease and neurodegeneration. He has served on numerous national and international grant review committees and has mentored and trained over 20 student and post-doctoral scientists. As the Herbert C. and Jacqueline Krieger Klein Endowed Chair in Alzheimer's disease and Neurodegeneration Research, Dr. D'Adamio will spearhead basic and translational research into Alzheimer's disease and neurodegeneration at Rutgers.



Keynote Speaker



Jie Shen, Ph.D.

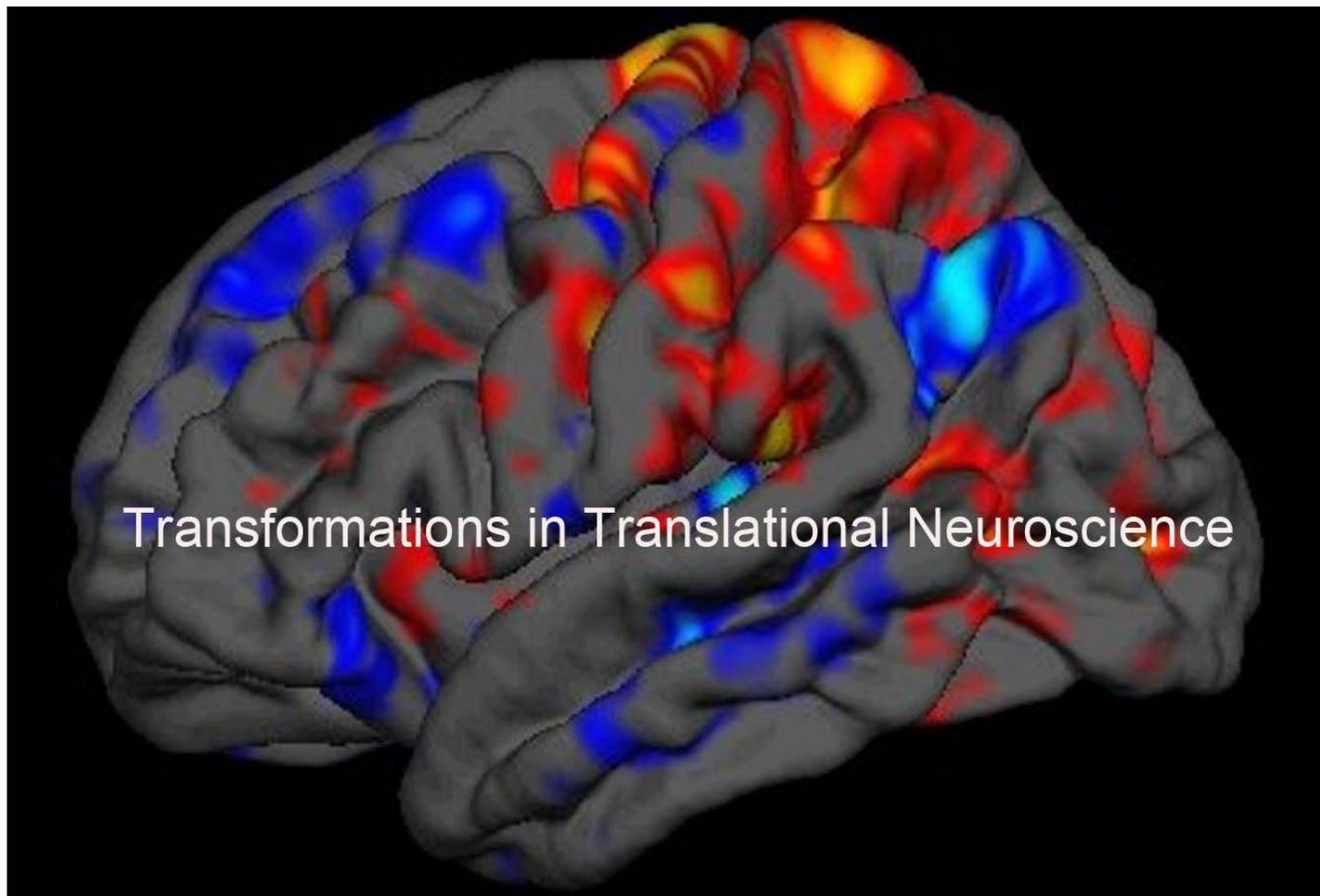
Professor

Director, Udall Center of Excellence for Parkinson's Disease
Brigham and Women's Hospital
Harvard Medical School

“Lessons from Genetic Studies of Alzheimer’s Disease”

Missense mutations in Presenilins and the amyloid precursor protein (APP) are linked to familial Alzheimer's disease (FAD). We employ gene targeting approaches in mice to investigate the normal physiological role of the Presenilin and APP families in the cerebral cortex and the dysfunction caused by Presenilin mutations. We also performed similar genetic analysis in Drosophila. Our genetic studies demonstrate that complete or partial inactivation of Presenilins in excitatory neurons of the adult cerebral cortex causes age-dependent increases in apoptosis and neurodegeneration, whereas similar conditional inactivation of APP family does not result in neurodegeneration. Furthermore, the essential role of Presenilin in support of neuronal survival in the aging brain is evolutionarily conserved, as conditional knockdown of the fly Presenilin homolog in adult neurons of the Drosophila brain also leads to age-dependent neurodegeneration. Interestingly, both Presenilin and APP families are required for normal synaptic plasticity in the mouse hippocampus, though the specific synaptic impairment observed in conditional knockout mice lacking either Presenilins or APP family members differ. We have also developed several lines of knockin mice expressing unique FAD mutations to investigate the pathogenic mechanism of FAD. Insight into novel disease mechanisms and their implications to AD therapeutic development will be discussed.

Dr. Shen's research focuses on elucidation of the pathogenic mechanisms of Alzheimer's and Parkinson's diseases. Her lab employs a multidisciplinary approach based on generation and analysis of mouse models, with the goal of understanding how pathogenic mutations perturb the normal *in vivo* function of gene products linked to these disorders. They discovered that the major Alzheimer's disease genes, presenilins, are essential for normal neuronal physiology and survival in the adult brain. Specifically, they found that presenilin inactivation causes striking age-dependent neurodegeneration that strongly resembles the neuropathology of Alzheimer's disease. Based on these and other findings, they proposed the novel hypothesis that presenilin mutations cause Alzheimer's disease through a loss-of-function pathogenic mechanism. Dr. Shen's lab has also generated mouse models for all genes thus far linked to autosomal recessive Parkinson's disease. Analysis of these mutant mice revealed important roles for the parkin, DJ-1 and PINK1 gene products in nigrostriatal dopaminergic physiology, suggesting that impaired dopamine release is a common pathophysiological alteration in the disease, and again pointing to impaired synaptic transmission as the initial trigger for neurodegeneration. Findings from her lab support the central hypothesis that synaptic dysfunction, and particularly impaired presynaptic neurotransmitter release, plays a crucial role in the pathogenic process leading to synaptic and neuronal loss.



Transformations in Translational Neuroscience



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