



Center for Neurodegenerative Disease Research
UNIVERSITY of PENNSYLVANIA

*“Focusing on Parkinson’s Disease Alpha-synuclein
at the University of Pennsylvania”*

Penn’s Center for Neurodegenerative Disease Research’s Annual

| MARIAN S. WARE |
RESEARCH RETREAT
2015

Chairs: Virginia M.-Y. Lee, PhD, MBA *and* John Q. Trojanowski, MD, PhD

Wednesday, October 7, 2015 | 8:30am - 5:00pm
Biomedical Research Building II/III Auditorium
Perelman School of Medicine at the
University of Pennsylvania



Center for Neurodegenerative Disease Research
UNIVERSITY *of* PENNSYLVANIA

presents

THE ANNUAL MARIAN S. WARE
RESEARCH RETREAT

***“Focusing on Parkinson’s Disease Alpha-synuclein
at the University of Pennsylvania”***

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AGENDA

- 8:30 AM **BREAKFAST BUFFET IN AUDITORIUM LOBBY (BRB II/III)**
- 9:00 AM **Opening Remarks: Virginia M.-Y. Lee, PhD, MBA**
Director, Center for Neurodegenerative Disease Research (CNDR)
Perelman School of Medicine at the University of Pennsylvania
- 9:15 AM **James Petersson, Associate Professor of Chemistry, School of Arts and Sciences**
“Synthetic protein modifications for studying the role of alpha-synuclein in Parkinson’s disease pathology”
- 9:40 AM **Zahra Fakhraai, Assistant Professor, Department of Chemistry, School of Arts and Sciences**
“High-resolution AFM Imaging of Amyloid Aggregates”
- 10:05 AM **James Shorter, Associate Professor, Department of Biochemistry and Biophysics, Perleman School of Medicine**
“Potentiated protein disaggregases to counter alpha-synucleinopathies”
- 10:30 AM **Elizabeth Rhoades, Associate Professor, Department of Chemistry, School of Arts and Sciences**
“The role of nascent helical structure in the function of alpha-synuclein”
- 10:55 AM **BREAK & POSTER VISITS**
- 11:10 AM **Kelvin Luk, Research Assistant Professor, Center for Neurodegenerative Disease Research**
“Interactions between alpha-synuclein across species”
- 11:35 AM **Richard Karpowicz, Postdoctoral fellow, Center for Neurodegenerative Disease Research**
“Shining light on the black box of pathological alpha-synuclein transmission”
- 11:50 AM **Anna Kashina, Professor of Biochemistry, School of Veterinary Medicine**
“Alpha synuclein arginylation facilitates normal brain health and prevents neurodegeneration”
- 12:15 PM **LUNCH & POSTER VISITS**
- 2:30 PM **Tobias Baumgart, Associate Professor, Department of Chemistry, School of Arts and Sciences**
“Biophysical effects on lipid membranes of peripheral protein binding”
- 2:55 PM **Harry Ischiropoulos, Research Professor of Pediatrics, Children’s Hospital of Philadelphia**
“Alarmins, immunoproteasome and autophagy; novel regulators of a-synuclein aggregation disorders”
- 3:20 PM **Mike Henderson, Postdoctoral fellow, Center for Neurodegenerative Disease Research**
“Other proteins implicated in synucleinopathies”
- 3:35 PM **Dustin Covell, Postdoctoral Fellow, Center for Neurodegenerative Disease Research**
“Conformational antibodies generated from alpha-synuclein fibril strains reveal distinct populations of pathological inclusions in Parkinson’s disease brain tissue”
- 3:50 PM **Bob Mach, Professor of Radiology, Perleman School of Medicine**
“Progress in the Development of a PET Radiotracer for Imaging Alpha Synuclein Aggregates in Parkinson’s Disease”
- 4:15 PM **Jon Toledo, Research Associate, Center for Neurodegenerative Disease Research**
“Data-Driven Characterization of α -Synuclein Deposition Patterns”
- 4:40 PM **Closing Remarks & Best Poster Award: Virginia M.-Y. Lee, PhD, MBA**
- 4:50 PM **CONCLUSION OF THE ANNUAL MARIAN S. WARE RESEARCH RETREAT**

E. JAMES PETERSSON, PHD

Associate Professor of Chemistry, University of Pennsylvania



E. James Petersson was educated at Dartmouth College, where he worked in the laboratory of David Lemal. He then studied under Dennis Dougherty at the California Institute of Technology as an NIH Predoctoral Fellow. After obtaining his Ph.D. in 2005, he trained as an NIH Postdoctoral Fellow at Yale University with Alanna Schepartz. He was appointed as Assistant Professor in the Department of Chemistry at the University of Pennsylvania in 2008 and in the Biochemistry and Molecular Biophysics group in the Perelman School of Medicine in 2013. In 2015, he was promoted to Associate Professor with tenure. His laboratory develops new methods for modifying proteins with synthetic probes in order to study their folding and stability. They apply these probes to problems of significant biomedical interest, including the aggregation of the Parkinson's disease protein, alpha-synuclein. For these contributions, Prof. Petersson has been the recipient of several awards, including a Sloan Fellowship, an NSF CAREER award, the Early Excellence in Physical Organic Chemistry award, and recognition as a Searle Scholar.

ZAHRA FAKHRAAI, PHD

Assistant Professor of Chemistry, University of Pennsylvania



Zahra received her B.Sc. and M.Sc. in physics from Sharif University of Technology in Iran. In 2003, she joined Jamie Forrest's group in University of Waterloo and studied the dynamics of polymers in thin films and on their surfaces. She received her PhD in Physics from the University of Waterloo in 2007, for which she received the American Physical Society's Padden award. From 2007 to 2008 Zahra worked in the Gilbert Walker's group at the University of Toronto and studied the structure and chemical composition of block copolymers and protein aggregates using near-field infrared imaging. Subsequently, Zahra moved to Mark Ediger's group at the University of Wisconsin-Madison (2009-2011) with an NSERC post-doctoral fellowship from the Canadian government. She joined Penn Chemistry in 2011, completing her transition from physicist to chemist. She now identifies herself as a material scientist interested in materials properties in small length scales and extremely slow dynamics.

Since joining Penn Chemistry Zahra and her group explored properties of materials at nanometer lengths scales. In 2014 Zahra received an NSF Career award to study the properties of glassy materials as interfaces and in nanometer lengths scale. The group is also interested in understanding the kinetics and self-assembly of peptides and proteins in two and three dimensional geometries and uses high-resolution atomic force microscopy to identify structure of amyloid aggregates. Zahra is the recipient of 2015 Sloan fellowship in Chemistry.

JAMES SHORTER, PHD

Associate Professor, Department of Biochemistry and Biophysics, University of Pennsylvania



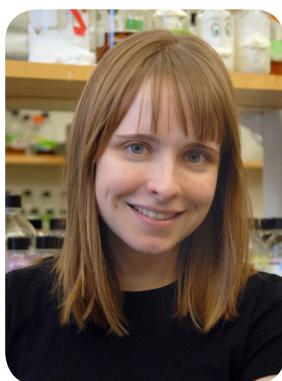
James Shorter is an Associate Professor of Biochemistry and Biophysics at the Perelman School of Medicine at the University of Pennsylvania. His research program aims to elucidate how to potentiate the proteostasis network to counter disease. They have elucidated mechanisms and pioneered the engineering of protein disaggregases to combat neurodegenerative disease. They have discovered the metazoan protein disaggregase system. They have also recognized that human RNA-binding proteins often harbor prion-like domains that misfold and cause neurodegenerative disease. They have also identified prion strain selection events can be driven by small-molecule drugs and protein disaggregases.

Website: www.med.upenn.edu/shorterlab/index.html

Twitter: twitter.com/shorterlab

ELIZABETH RHOADES, PHD

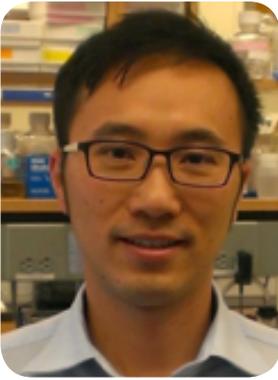
Associate Professor of Chemistry, University of Pennsylvania



Dr. Rhoades completed an undergraduate degree in Physics at Duke University, and a PhD in Biophysics from the University of Michigan. Following postdoctoral work at the Weizmann Institute of Science and Cornell University studying protein folding and aggregation, she spent 9 years as a professor in the Department of Molecular Biophysics & Biochemistry at Yale University. She joined the Chemistry Department at the University of Pennsylvania in July 2015. Research in the Rhoades group is focused on intrinsically disordered proteins, including α -Synuclein, tau, islet amyloid polypeptide, and tau. The group uses a wide variety of biochemical and biophysical approaches, but specializes in single molecule fluorescence methods.

KELVIN LUK, PHD

Research Assistant Professor, Center for Neurodegenerative Disease Research



Dr. Luk is currently Research Assistant Professor of Pathology and Laboratory Medicine at the University of Pennsylvania's Center for Neurodegenerative Disease Research. His research strives to understand the relationship between the formation of alpha-synuclein pathology that characterizes Parkinson's disease (PD) and its role in neuronal dysfunction and degeneration. Using a multidisciplinary approach spanning in vitro, cell-based, and in vivo models, his team has been interrogating the mechanisms by which misfolded forms of this protein act as pathological agents that self-propagate and spread throughout the CNS. Dr. Luk is also a member of the CNDR's Drug Discovery Group and contributes to its efforts in identifying potential therapeutic strategies for PD and related neurodegenerative disorders.

Dr. Luk received his B.Sc. in 1997 (Microbiology and Immunology) and Ph.D. (Pathology) from McGill University. He completed his postdoctoral training at the University of Pennsylvania, under the mentorship of Dr. Virginia Lee. He obtained a Masters in Translational Research from Penn in 2013.

RICHARD KARPOWICZ, PHD

Postdoctoral Fellow, Center for Neurodegenerative Disease Research



Rich Karpowicz is a Postdoctoral Researcher at the Center for Neurodegenerative Disease Research at the University of Pennsylvania. He received his BS in Biochemistry from the University of Delaware, where he was a Pfizer Undergraduate Researcher in Organic Synthesis. He completed his PhD at Columbia University in the Department of Chemistry, where he worked on the development of advanced Fluorescent False Neurotransmitters to act as specific optical tracers of monoamine neurotransmitters in brain tissue and cultured cells.

At CNDR, Rich is developing new experimental techniques to address the poorly understood processes governing cell-to-cell transmission of synuclein and tau pathology. Specifically, he is interested in mechanisms by which neurons take up proteopathic seeds, how these seeds are processed and trafficked, and what events lead to recruitment of soluble protein and the ultimate development of pathology. His overarching motivation is to apply his background in chemistry and chemical biology to the development of new techniques to understand the brain and its diseases.

ANNA KASHINA, PHD

Professor of Biochemistry, School of Veterinary Medicine, University of Pennsylvania



Anna Kashina's research focuses on investigating the physiological role of protein arginylation, an emerging posttranslational modification of global significance. Her work demonstrated that knockout of the enzyme responsible for arginylation, ATE1, leads to embryonic lethality in mice with defects in heart development and angiogenesis, and that arginylation regulates many proteins involved in cytoskeleton, cell motility, signaling, and metabolism. Her most recent discovery revealed a new mechanism of modification of intact proteins via arginylation of acidic side chains of Asp and Glu and uncovered that one of the proteins prominently modified through this mechanism is alpha synuclein, the key player in neurodegeneration. Dr. Kashina's ongoing research is aimed to uncover new pathways of protein regulation and new potential therapeutic approaches to be explored in treatment of heart disease, cancer, and neurodegeneration.

TOBIAS BAUMGART, PHD

Associate Professor, Department of Chemistry, University of Pennsylvania



Tobias Baumgart, PhD has a broad background in physical chemistry, with an emphasis on membrane biophysics. As a postdoctoral researcher with Watt Webb (Applied and Engineering Physics), Gerald Feigenson (Biochemistry), and Barbara Baird (Chemistry and Chemical Biology) at Cornell University, he further broadened his background in molecular biology and cell biology. Also at Cornell University, Dr. Baumgart worked closely with theoretical engineers in developing and applying analytical models to the interpretation of his experimental data.

His research at the University of Pennsylvania is largely focused on characterizing the function of membranes. He collaborates with theoretical physicists, theoretical and experimental engineers, protein biophysicists and cell biologists, to achieve their mutual research goals and has demonstrated leadership and productivity as a PI on multiple NIH and NSF funded grants.

HARRY ISCHIROPOULOS, PHD

Research Professor of Pediatrics, Children's Hospital of Philadelphia



Harry Ischiropoulos is the Gisela and Dennis Alter Research Professor of Pediatrics and Systems Pharmacology and Translational Therapeutics at the Children's Hospital of Philadelphia Research Institute and the Perelman School of Medicine at the University of Pennsylvania. His laboratory investigates the biological chemistry and signaling pathways of nitric oxide in the cardiovascular and neuronal systems. They also employ mass spectroscopy-based technologies to study the aggregation and neurotoxicity of α -synuclein in cellular and mouse models.

MIKE HENDERSON, PHD

Postdoctoral Fellow, Center for Neurodegenerative Disease Research



Mike Henderson began his science career as an undergraduate in the laboratory of Dr. Debra Fadool, where he successfully defended his thesis titled "Glucose and diet-induced obesity modulation of ion channel biophysics." He graduated magna cum laude from Florida State University in 2008 with a B.S. in Biology.

From there, he joined the Interdepartmental Neuroscience Program at Yale University in the laboratory of Dr. Sreeranga Chandra. He studied the role of cysteine string protein α in synapse maintenance and the neurodegenerative disease adult-onset neuronal ceroid lipofuscinosis. He successfully defended his thesis titled "The role of presynaptic co-chaperone CSP α regulation in neurodegeneration."

In 2014, Mike joined the Center for Neurodegenerative Disease Research at the University of Pennsylvania as a postdoctoral fellow in the laboratory of Drs. Virginia Lee and John Trojanowski. Here, he studies models of Parkinson's disease with the goal of understanding pathogenesis and developing therapeutics for this devastating disease.

DUSTIN COVELL, PHD

Postdoctoral Fellow, Center for Neurodegenerative Disease Research



Dr. Covell graduated with a BA in chemistry and an emphasis in neuroscience in 2005 from Macalester College in St. Paul, MN. He then attended the University of Illinois at Urbana-Champaign for his doctoral work in the lab of Prof. M. Christina White. After completing his PhD in organic chemistry in 2011, he moved to the Center for Neurodegenerative Disease Research to begin his post-doctoral research. His research interests include investigating the chemical level functioning of the healthy and diseased brain with the aim of developing therapies for the treatment of neurological disorders.

ROBERT H. MACH, PHD

Professor of Radiology, Perelman School of Medicine University of Pennsylvania



Robert H. Mach obtained a B.A. degree in chemistry from the State University of New York-College at Potsdam in 1978 and a Ph.D. degree from the Department of Medicinal Chemistry, School of Pharmacy of the State University of New York at Buffalo in 1985. He entered the field of radiopharmaceutical chemistry in 1985 by joining the laboratory of Dr. Hank F. Kung of the Department of Nuclear Medicine of SUNY-Buffalo. In Dr. Kung's laboratory, he worked on the development of ^{99m}Tc -labeled fatty acids for myocardial imaging and ^{123}I -labeled radiotracers for imaging CNS receptors. After moving with Dr. Kung to the University of Pennsylvania in 1987, Dr. Mach joined the PET Program at PENN in 1988. He moved to Wake Forest University School of Medicine in 1992, where he was appointed as an Assistant Professor in the Departments of Radiology and Physiology & Pharmacology. He was promoted to an Associate Professor in 1995 and Professor in 2000, and was named Vice Chairman for Research in the Department of Radiology of WFUSM in 2000. His key scientific accomplishment at WFUSM was the demonstration of effects of acute and chronic cocaine self-administration and chronic socially-derived stress on dopamine receptor function in nonhuman primate models of behavior with PET.

In the summer of 2002, Dr. Mach moved to the Division of Radiological Sciences of Washington University School of Medicine where he was a Professor in the Departments of Radiology, Cell Biology & Physiology, and Biochemistry & Molecular Biophysics. Dr. Mach was also the Director of the Washington University Cyclotron Facility (2004 – 2013) and Chief of the Radiological Chemistry Lab (2007 – 2013) of the Mallinckrodt Institute of Radiology. At WUSM, his key scientific accomplishment was the development of 6 different PET radiotracers which are currently being used in clinical trials. In 2013, he returned to the University of Pennsylvania and is the Britton Chance Professor of Radiology and Director of the PET Radiochemistry Program. His research interests include the development of radiotracers for imaging CNS receptors, cell proliferation, and mechanisms of cellular death. He has over 190 peer review publications, 10 book chapters, and holds 20 patents on the development of PET-based radiopharmaceuticals.

JON TOLEDO, PHD

Research Associate, Center for Neurodegenerative Disease Research



Jon Toledo graduated from University of Navarra School of Medicine and did his Neurology training in the University Clinical Hospital of Navarra. Since 2011 he has been working as a postdoctoral fellow in the Center for Neurodegenerative Disease Research at the University of Pennsylvania and in 2014 he was promoted to Research Associate.

He studies neurodegenerative diseases, mainly Alzheimer's disease and Lewy body disease (encompassing Parkinson's disease - with and without dementia - and dementia with Lewy bodies) and the overlap of different neurodegenerative and non-neurodegenerative diseases in subjects with dementia. His studies combine cerebrospinal fluid, neuroimaging, neuropathological and clinical measures to model disease progression and biomarker changes and predict clinical outcomes.

In this field, his main interests are the identification of coincident neuropathologies using multi-modal biomarkers and the characterization of disease endophenotypes that lead to an individualized approach to disease. He has authored 57 publications in peer-reviewed journals, written seven book chapters and is a reviewer for 18 journals in the field of neuroscience.”

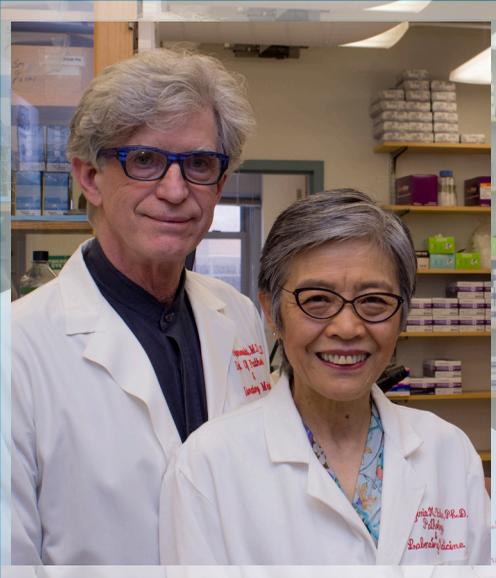
ACKNOWLEDGEMENTS

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- William Maul-Measey Foundation
- National Institute on Aging of the National Institutes of Health (Training Program in Age-related Neurodegenerative Diseases)
- The Penn Alzheimer's Disease Core Center
- The Institute on Aging, Perelman School of Medicine at the University of Pennsylvania
- The Penn Memory Center, University of Pennsylvania
- Penn Frontotemporal Degeneration Center
- The Penn Parkinson's Disease and Movement Disorders Center at Pennsylvania Hospital
- National Institute of Neurological Disorders and Stroke (NINDS)
- Morris K. Udall Parkinson's Disease Research Center of Excellence at the University of Pennsylvania
- Parkinson's Disease Research, Education and Clinical Centers (PADRECC) at the Corporal Michael J. Crescenzo VAMC
- *Support of the friends and families of our patients who have made our research possible.*

ABOUT CNDR

The **Center for Neurodegenerative Disease Research** (CNDR) is a “center without walls” wherein University of Pennsylvania investigators collaborate in the study of aging-related neurodegenerative diseases.

The mission of CNDR is to conduct multidisciplinary clinical and basic research studies to increase the understanding of the causes and mechanisms leading to brain dysfunction and degeneration in Alzheimer’s disease (AD), Parkinson’s disease (PD), Frontotemporal degeneration (FTD), Amyotrophic lateral sclerosis (ALS) and other neurodegenerative disorders that occur with advancing age.



Drs. Virginia M.-Y. Lee, Director, and ***John Q. Trojanowski***, Co-director, established CNDR at the University of Pennsylvania in 1991 to pursue the far-reaching goals of developing new and more effective therapies for these devastating diseases.

They have garnered support for their research from the National Institutes of Health (NIH), especially National Institute on Aging (NIA), National Institute of Neurological Disorders and Stroke (NINDS), and the Alzheimer’s Association. CNDR is the home base of the NIA-funded Alzheimer’s Disease Core Center and NINDS-funded Morris K. Udall Parkinson’s Disease Research Center of Excellence.

CONTACT CNDR



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RESEARCH PROGRAMS & PARTNERSHIPS

The Marian S. Ware Alzheimer's Program

Penn Alzheimer's Disease Core Center

Penn Memory Center

Penn Udall Center for Parkinson's Research

Institute on Aging

Penn Frontotemporal Degeneration Center

The Penn Parkinson's Disease and Movement Disorders Center
at Pennsylvania Hospital

Parkinson's Disease Research, Education and Clinical Centers
(PADRECC) at the Corporal Michael J. Crescenzo VAMC

Center for Neurodegenerative Disease Research

Department of Pathology and Laboratory Medicine

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