

THE SCIENCE OF AGING

FALL 2022

// An Institute on Aging Newsletter

GENETIC VARIANT, TREM2, ASSOCIATED WITH ATYPICAL ALZHEIMER'S DISEASE

A University of Pennsylvania-led research study suggests that the rare genetic variant, TREM2, increases one's risk of Alzheimer's disease (AD) but also causes atypical symptoms. This finding could have a significant impact on how AD is diagnosed.

"We were able to demonstrate, with the largest brain autopsy study of cases with this genetic risk variant to date, that TREM2 variants are associated with these atypical Alzheimer's disease symptoms," said **Edward Lee, MD, PhD**, Co-director of the Institute on Aging (IOA) and Co-associate director of the University of Pennsylvania's Alzheimer's Disease Research Center (ADRC).

The study used 54 cases with 14 different types of TREM2 variants identified from the Center for Neurodegenerative Disease Research (CNDP) brain bank at Penn. Researchers gathered genetic, demographic, and diagnostic information to better understand how TREM2 works in patients with AD. When patients had the TREM2 variant, the team found that they often had a faster cognitive decline.

The team also compared the neuropathology, or brain tissue, between those with and without TREM2. These findings confirmed that even with atypical symptoms, many patients with the TREM2 variant do have AD.

"We did not see any difference in amyloid or the amount of tau," said **Boram Kim**, a postdoctoral fellow in the Translational Neuropathology Research Laboratory at the Perelman School of Medicine, University of Pennsylvania and lead author of the study. "But the spreading patterns of tau varied."

"Not only will this potentially help guide a personalized approach to dementia diagnosis, this study provides useful insights into the basic processes that lead to dementia," said Dr. Lee.

This research study was published in *Acta Neuropathologica*.

// By Meghan McCarthy, Penn Memory Center

A LOOK INSIDE

Introducing IOA Divisions

Learn about the IOA's four new Divisions and the Penn faculty leading them

IOA Retreat 2022: Fluid Biomarkers in AD

Meet our IOA PennPREP Scholar

ABOUT THE IOA'S NEW MEMBERS PROGRAM



Institute on Aging
UNIVERSITY OF PENNSYLVANIA

INTRODUCING IOA DIVISIONS



With the recent leadership transition, the IOA has the opportunity to refresh its organizational structure. In alignment with its mission to improve the health of older adults by increasing the quality and quantity of clinical and basic research as well as educational programs focusing on normal aging and aging-related diseases across the entire Penn campus, the IOA will focus its efforts in four main areas, or IOA Divisions.

Each division is led by members of the Penn faculty with expertise in their designated division who will serve liaisons for potential collaboration within the organization and help shape future IOA initiatives.

» Division of Basic Neurodegenerative Disease Research

This division focuses on basic, mechanistic research into the pathophysiology of neurodegenerative diseases including Alzheimer's disease and related dementias (frontotemporal degeneration, dementia with Lewy bodies), movement disorders, and motor neuron diseases. The key strengths and focus of this division have been in biochemistry, genetics, and pathology.

Division Leader: Edward B. Lee, MD, PhD

"My goal is to bring together world-class scientists by promoting the cross fertilization of diverse ideas, fostering successful collaborations, and recruiting the most promising trainees and faculty to the University of Pennsylvania in order to discover the causes and cures of aging-related neurodegenerative diseases."

– Eddie Lee, MD, PhD



» Division of Clinical and Translational Neurodegenerative Disease Research

This division focuses on translational and clinical research on neurodegenerative diseases including Alzheimer's disease and related dementias (frontotemporal degeneration, dementia with Lewy bodies), movement disorders, and motor neuron diseases. The key strengths and focus of this division include biomarker development and validation (biofluid, neuroimaging, multimodal integration), studies on the structure and function of the aging brain (neuropsychology, clinical outcomes, neuroimaging), and the development of care models. This division encourages an emphasis on translating basic research into clinical trials and practice.

Division Leader: David A. Wolk, MD



"The IOA has played a key role in my and many other careers at Penn by providing a forum for exchange of ideas, opportunities to present data and meet outside investigators, and recruitment of collaborative faculty. I would like the IOA to continue to serve as a milieu and forum for supporting the broad study of aging at Penn and to integrate and leverage the various lenses in which aging and age-related diseases are studied to promote healthier and happier aging."

– David A. Wolk, MD

» Division of Geroscience, Gerontology, and Geriatrics

This division focuses on basic, translational, and clinical research on human aging including basic molecular alterations (telomere biology, epigenetics, metabolism) and clinical phenotypes (frailty, integrated care models, metabolism).

Division Leaders: F. Bradley (Brad) Johnson, MD, PhD, and Anne Cappola, MD, ScM

"Penn has deep yet diverse strengths spanning studies into the fundamental causes of aging to investigations of the nature of the many diseases for which aging puts people at a dramatically elevated risk. I hope to help continue the IOA's past successes of fostering collaboration among investigators across this spectrum to enhance human wellbeing into old age."

– Brad Johnson, MD, PhD



"Geroscience weaves together the basic and clinical science in aging, working together to study the underpinnings of chronic disease, frailty, and resilience. The IOA is the home for investigators performing research across these areas."

– Anne Cappola, MD, ScM

» Division of Epidemiology, Social Science, and Policy

This division focuses on social, ethical, and legal scholarship in addition to population science and epidemiology as it relates to neurodegenerative diseases and aging. These include research on understudied populations (global, underrepresented), the social impact of aging-related diseases, ethical and health economics considerations in aging and neurodegenerative disease and their interface with policy and legal frameworks.

Division Leader: Norma Coe, PhD

"I look forward to helping to make connections between the social scientists and the bench scientists studying aging. Bench science discoveries are pushing the social sciences forward, such as studying the socioeconomic gradient in epigenetic clocks to help identify the social factors that contribute to biologic measures of aging. And we are only touching the tip of the iceberg."

– Norma B. Coe, PhD



FLUID BIOMARKERS: THE NEXT WAVE OF DIAGNOSTIC TOOLS IN ALZHEIMER'S DISEASE

This year's IOA Sylvan M. Cohen Annual Retreat focused on fluid biomarkers, the next wave of diagnostic tools in Alzheimer's disease (AD).

Topics covered included an update on biofluid-based biomarkers for amyloid and neurodegeneration by **Henrik Zetterberg, MD, PhD**, professor at the University of Gothenburg, Sweden, and University College London, and plasma tau biomarkers in acute and chronic neurological diseases by **Thomas Karikari, PhD**, assistant professor at the University of Pittsburgh.

"Biomarkers are an important part of dementia research. They help researchers detect early brain changes, better understand how risk factors are involved, identify participants who meet particular requirements for clinical trials and studies, and track participants' responses to a test drug or other intervention, such as physical exercise."

- nia.nih.gov

Several Penn presenters also shared their research in the field. This year's lineup included **Katheryn A.Q. Cousins, PhD**, **Tom Tropea, DO, MPH, MTR**, **Les Shaw, PhD**, **Jina Ko, PhD**, and **Ramon Diaz-Arrastia, MD, PhD**.

"My hope is that we develop biomarkers for non-AD pathologies," said **Eddie Lee, MD, PhD**, neuropathologist and co-director of the IOA, when asked about his thoughts on the future of biomarkers in AD research. "We desperately need things for TDP-43, alpha-synuclein, other proteinopathies."

Full presentations from the event are available for viewing on our website.



MEET OUR FIRST IOA PENNPREP SCHOLAR

The University of Pennsylvania Post-Baccalaureate Research Education Program (PennPREP) offers a one-to-two-year research experience for students, who have completed their bachelor's degree, are interested in pursuing a doctoral degree in the biomedical sciences, and would benefit from protected time to develop additional skills research. The program provides a full time research experience in a biomedical science discipline, along with preparation for applying to and succeeding in graduate school.

PennPREP is one of many PREP initiatives across the country meant to increase STEM diversity, specifically targeting Black/African-Americans, Hispanic/Latino/Chicano Americans, Native Americans and Alaskan Natives, and Pacific Islanders.

As part of the IOA's recent restructure, one of our new endeavours is to support a student in the program as an IOA PennPREP Scholar. Meet our first IOA PennPREP Scholar, **Lauryn Brooks**.



Working in the lab of Dr. Foteini Mourkioti in the McKay Department of Orthopedic Research, Brooks is currently studying the Mechanosensing Ion Channel, Piezo 1, and its role in skeletal muscle function. Piezo 1 regulates the influx of calcium ions into the cell as calcium is essential to muscle contractions. Using mouse models to knock out Piezo 1 in muscle fiber, Brooks is studying how the lack of Piezo 1 affects muscle fiber physiology and function, and how this may be affected by aging.

"I aspire to become a physician-scientist and continue to work in the field of bioengineering," said Brooks. "PREP has given me the opportunity to conduct research, shadow physicians, and take graduate-level courses which will bolster my future graduate school applications."

Lauryn Brooks graduated with a B.S. in Biochemistry from Hampton University in May 2022 and has held many internships in a wide range of disciplines gaining experience from the National Institutes of Health, the Broad Institute of Harvard and MIT, Michigan State, and the Seattle Structural Genomics Center for Infectious Disease.

MISSION

The mission of the Institute on Aging (IOA) at the University of Pennsylvania is to improve the health of older adults by increasing the quality and quantity of clinical and basic research as well as educational programs focusing on normal aging and aging-related diseases across the entire Penn campus.

CONTACT

3615 Chestnut Street
Philadelphia, PA 19104

215-898-7801

aging@pennmedicine.upenn.edu

LEARN MORE

Learn more about the IOA, including our annual events and Members Program at:

www.med.upenn.edu/aging

CONNECT



/ Penn Aging



/ Penn Aging



/ Penn Institute on Aging



/ Penn Institute on Aging

INTRODUCING THE IOA MEMBERS PROGRAM

Are you a Penn faculty member (or know someone who is!) interested in aging and/or neurodegenerative disease research?

Join our new IOA Members program!

Benefits of IOA Membership:

- Potential funding of IOA Post-doctoral fellows
- Potential funding of IOA PennPREP Scholar(s)
- Identification of potential invited speakers to present at the IOA Seminar Series
- Priority for scheduled meetings with IOA Seminar Series speakers
- Trainees eligible to present at IOA-sponsored trainee seminars
- Trainees eligible to attend IOA-sponsored career development activities
- Participate in shaping the future of aging research at Penn

Each IOA Member must identify with AT LEAST ONE of the four new IOA Divisions:

- Division of Basic Neurodegenerative Disease Research
- Division of Clinical and Translational Neurodegenerative Disease Research
- Division of Geroscience, Gerontology, and Geriatrics
- Division of Epidemiology, Social Science, and Policy

FULL STORIES AVAILABLE AT: WWW.PENNINSTITUTEONAGING.WORDPRESS.COM

MEDICINE
HEALTH
TREATMENT
DOCTOR
SURVEY
SCIENCE



Institute on Aging
UNIVERSITY OF PENNSYLVANIA