# THE SCIENCE OF AGING

*Winter 2018*




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*The mission of the Institute on Aging 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.*

Institute on Aging
University of Pennsylvania

## THE JOSEPH A. PIGNOLO AWARD IN AGING RESEARCH | 2017

*"Mitochondrial-targeted catalase is good for the old mouse proteome, but not for the young: 'reverse' antagonistic pleiotropy?"*

On Wednesday, November 29, 2017, the Institute on Aging (IOA) hosted their annual **Joseph A. Pignolo Award in Aging Research**. This year's speaker, **Nathan Basisty, PhD**, a postdoctoral research fellow at The Buck Institute for Research on Aging, received the award for his 2016 paper "Mitochondrial-targeted catalase is good for the old mouse proteome, but not for the young: 'reverse' antagonistic pleiotropy?" published in *Aging Cell*.

Dr. Basisty's research focuses heavily on the role of protein homeostasis in aging. Protein homeostasis is the process by which a cell retains an equilibrium of proteins to maintain its proper functions. According to a 2013 publication in *Nature*, it is believed that "a cell's failure to maintain proper protein homeostasis has a major role in ageing and age-related diseases" *(Nature Reviews Molecular Cell Biology 14, 55-61 (2013) BH Toyama and MW Hetzer)*. Dr. Basisty and his team are also looking at the role of this process in longevity with several interventions intended to extend lifespan in mammals.

**Learn more about Dr. Basisty's research and future goals in our short video interview at:**
www.penninstituteonaging.wordpress.com

**Left to right**: John Q. Trojanowski, MD, PhD, Director, IOA; Nathan Basisty, PhD, Pignolo Awardee; Robert J. Pignolo, MD, PhD, Chair, Geriatric Medicine and Gerontology, Mayo Clinic College of Medicine

## WHICH AGING-RELATED DISEASE DO YOU FEAR MOST?

☐ CANCER ☐ HEART DISEASE ☐ ALZHEIMER'S DISEASE

If you were faced with this question, which option would you choose?

The Institute on Aging conducted a small video poll to find out how people of all ages, races, and genders on and around the University of Pennsylvania's campus would respond. Over the course of three hours of filming, 32 people agreed to answer our question on camera with no prompting or background information. Over 65% of people answered Alzheimer's disease.

Some participants shared that they have seen first-hand just how debilitating Alzheimer's can be while watching loved-ones live with the disease and that they fear that they may be at risk due to family history. Others were less familiar with the specifics but simply fear losing their memories and sense of self. However, regardless of their experiences, or lack-thereof, with Alzheimer's disease, most were shocked to learn just how prevalent it is.

According to the Alzheimer's Association, since 2000, deaths from heart disease have decreased by 14% while deaths from Alzheimer's have increased by 89%. It is the 6th leading cause of death in the United States and kills more than breast cancer and prostate cancer combined (www.alz.org). Still, funding for Alzheimer's disease research is severely lacking in comparison to other aging-related diseases like cancer and heart disease.

In fiscal year 2016, the National Institutes of Health (NIH) funding for cancer was $5,598 million and $1,289 million for heart disease with a mere $175 million for Alzheimer's disease.

There are currently an estimated 5 million Americans living with Alzheimer's disease and unless more is done to combat this disease, that number could rise as high as 16 million by 2050.

**To learn more and help raise awareness by sharing our video, visit:**
**www.penninstituteonaging.wordpress.com**

*Tips to help*

# AVOID COLD STRESS

### Courtesy of the Philadelphia Corporation for Aging

The elderly population is disproportionately affected by hypothermia (commonly known as cold stress), caused by excessive body heat loss and exposure to cold. Those who don't dress warmly enough; live in a cold room or house; lack shelter from the snow, rain, wind, and water; eat poorly and take certain prescription medications are at risk for cold stress. Cold stress can happen indoors, even at temperatures as mild as 60°- 70°F. People can help protect themselves by following some simple guidelines, according to **Sharon Congleton, R.N., B.S.N**., health promotion nurse supervisor at Philadelphia Corporation for Aging (PCA).

**TIPS:**

- Stay warm and dry, indoors and outdoors
- Avoid exposure to snow, wind, rain and water/dampness
- Dress warmly
  - *Wear loose layers of clothing, especially woolens*
  - *Cover head and neck (wear hat and scarf)*
  - *Wear gloves or mittens*
  - *Change socks and long underwear if they become damp or wet*
  - *Wear warm shoes and socks*
- Keep skin and clothing dry to lessen the chance of frostbite
- Eat nutritious meals, especially a hot meal, on a regular basis
- Drink plenty of fluids

If taking medication for high blood pressure, nervousness, depression, poor circulation or sleeplessness, talk about hypothermia/cold stress with your doctor.
Learn more about the PCA at PCACares.org

### What to do in an Emergency:

- DO call 9-1-1 for medical assistance
- DO cover head and neck
- DO wrap in blankets, towels, extra clothes, or newspaper
- DO handle the person gently
- DO warm the person gradually
- DO take off wet clothes and provide warm, dry clothing

### What NOT to do in an Emergency:

- DO NOT give hot drinks or hot food
- DO NOT give alcohol or medications
- DO NOT bathe or shower
- DO NOT rub or massage arms or legs

## WOMEN WITH PARKINSON'S DISEASE LESS LIKELY THAN MEN TO HAVE CAREGIVERS // Penn Medicine News Release

Female Parkinson's disease patients are much less likely than male patients to have caregivers, despite the fact that caregivers report greater strain in caring for male patients. The findings come from a large study reported in Neurology by researchers at the Perelman School of Medicine at the University of Pennsylvania. According to the study, the disparity between female and male patients probably derives in part from the fact that women tend to outlive their most likely potential caregivers: their husbands.

**Nabila Dahodwala, MD**, associate professor of Neurology at Penn Medicine, and her colleagues' analysis was part of a larger study of Parkinson's patients, funded by the National Parkinson's Foundation (NPF), that has been ongoing since 2009 at Penn Medicine and 20 other centers in the U.S., Canada, the Netherlands, and Israel. The analysis covered 7,209 patients enrolled during 2009-2014.

The researchers found that 88.4 percent of male patients reported having a caregiver at the time they were enrolled in the NPF study, compared to just 79.4 percent of female patients. Male patients also were more likely to have a caregiver accompany them on their first visit to a study center (61.0 percent vs 56.8 percent). These support-related disparities between male and female patients remained obvious even when the researchers adjusted the analysis to account for small differences between the patient groups in average age, disease duration and other variables.

> *"Changes in health policy to better support older women with disabilities are urgently needed."*
> *- Nabila Dahodwala, MD*

The study was not designed to determine the underlying reasons for disparities in caregiver support, but as Dahodwala noted, "prior studies across multiple disabling conditions have found that women are less likely than men to have caregiver support."

Women on average live a few years longer than men, and so are more likely when elderly to be living alone rather than with a spouse/caregiver, she added. Moreover, women generally are much more likely than men to be caregivers, hinting that even married female patients whose husbands are still living are less likely to receive care from them, compared to vice-versa. Consistent with these possibilities, Dahodwala and colleagues found in the study that 84 percent of the male patients reported having their spouse as caregiver, compared to just 67 percent of the female patients. The female patients also were more than twice as likely (3.0 percent vs. 1.3 percent) to have a paid caregiver.

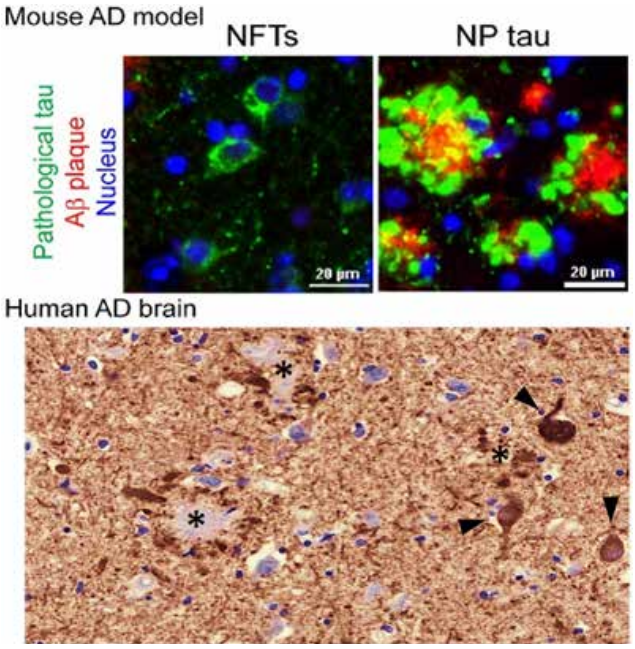
Dr. Dahodwala and her colleagues are now following up with a study designed to identify more precisely the causes of sex disparities in caregiver support for Parkinson's patients, and to find ways to correct those disparities. "Our overall goal is to develop tailored interventions to support caregivers and, in particular, to design innovative programs to improve outcomes for women with Parkinson's disease," she said.

**For the full Penn Medicine news release, visit**: https://www.pennmedicine.org/news/news-releases/2017/december

# New Alzheimer's Animal Model More Closely Mimics Human Disease

A Penn Medicine News Release by Karen Kreeger

By injecting human Alzheimer's disease brain extracts of pathological tau protein (from postmortem donated tissue) into mice with different amounts of amyloid-β (Aβ) plaques in their brains, researchers from the Perelman School of Medicine at the University of Pennsylvania found that amyloid-β facilitates the interaction between the plaques and abnormal tau. This relationship promotes the spread of mutated tau proteins in neurons, which is the hallmark of long-term Alzheimer's disease. They recently published their findings in *Nature Medicine*.




**Upper panel**: Tau clumps in new AD mouse model, either in the cell body as neurofibrillary tangles (NFTs) or in dystrophic axons surround A-beta plaques as neuritic plaque tau (NP tau). Lower panel: tau clumps in human AD brain, as NFTs (arrow head) and NP tau.
**Credit:** The lab of Virginia Lee, PhD, Perelman School of Medicine, University of Pennsylvania

"Making an AD mouse model that incorporates both Aβ and tau pathologies in a more AD-relevant context has been greatly sought after but difficult to accomplish," said senior author **Virginia M-Y Lee, PhD**, director of the Center for Neurodegenerative Disease Research (CNDR) at Penn. "This study is a big step for AD research, which will allow us to test new therapies in a more realistic context."

Alzheimer's disease is characterized by Aβ plaques outside cells and clumps of tau within cells. Researchers have proposed that Aβ plaques are the initiating pathology of AD, but the failure of all AD clinical trials based on removing Aβ challenges this hypothesis and the idea of targeting Aβ alone to treat AD. At the same time, evidence from other studies, including research from CNDR, strongly correlates the spread of tau clumps with worsening cognition in AD, but the exact link between the two pathologies has remained enigmatic.

Tau works like railroad track crossties in stabilizing microtubules in axons responsible for transporting material inside neurons. Removal of tau protein from microtubules due to its clumping in nerve cells causes the affected neurons to become dysfunctional, ultimately leading to their death and AD.

The Penn team mimicked the formation of three major types of AD-relevant tau pathology in their new mouse model: neurofibrillary tangles, neuropil threads, and tau aggregates surrounding Aβ plaques, called neuritic plaque tau. "For the first time we could see and study the tau clumps in dystrophic axons surrounding Aβ plaques in a mouse model, just like we see in a human brain with AD," said first author **Zhuohao He, PhD**, a postdoctoral fellow in Lee's lab.

The team found that Aβ plaques create an environment that facilitates the rapid amplification and spread of pathological tau into large aggregates, initially appearing as neuritic plaque tau. This was followed by the formation and spread of neurofibrillary tangles and neuropil threads to other neurons. These tau protein formations also impaired brain functions, including memory difficulties, in the mice.

This study is the basis for a new way to explain how the Aβ plaque environment accelerates the spread of tau pathology in the brains of AD patients, which is consistent with imaging studies and investigations of postmortem AD brains. The findings suggest new targets and strategies to treat AD patients. "Our new mouse model of AD with both Aβ and tau can now be used to test therapies that target one or both pathologies to see if combination or single-target therapy is better," Lee said.


## Apply Now: FY 2019 IOA/ADCC Pilot Awards

The University of Pennsylvania Institute on Aging (IOA) and Alzheimer's Disease Core Center (ADCC) Pilot Award Applications for fiscal year (FY) 2019 are now open!

Deadline: February 2, 2018.

Download the RFA at:
https://www.med.upenn.edu/aging/PilotAwards.html

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## UPCOMING EVENTS

**February 6, 2018**
**Vincent J. Cristofalo Annual Lectureship**
**Keynote Speaker**: Tom Misteli, PhD, *Director, Center for Cancer Research, National Cancer Institute*
3:00 - 4:00pm | Smilow Center | Arthur H. Rubenstein Auditorium
*3400 Civic Center Boulevard, Philadelphia, PA 19104

**March 7, 2018**
**IOA Visiting Scholars Series: Henry Paulson, MD, PhD**
*Lucile Groff Professor of Neurology, Director, Michigan Alzheimer's Disease Center*
3:00 - 4:00pm | Smilow Center* | Arthur H. Rubenstein Auditorium

**April 3, 2018**
**IOA Visiting Scholars Series: Edward Huey, MD**
*Assistant Professor of Psychiatry and Neurology, Taub Institute for Research on Alzheimer's Disease and the Aging Brain, Columbia University*
3:00 -4:00pm | Biomedical Research Building (II/III) Auditorium
421 Curie Boulevard, Philadelphia, PA 19104

**May 1, 2018**
**Sylvan M. Cohen Annual Retreat and Poster Session: "Impact of life course exposures on aging: Longevity reflects our experiences from day to day"**
**Keynote Speaker:** Kenneth M. Langa, MD, PhD, *Professor Internal Medicine, Gerontology, and Health Management and Policy, University of Michigan*
**Co-sponsors:** The Population Aging Research Center (PARC)
11:30am - 5:00pm | Smilow Center* | Arthur H. Rubenstein Auditorium

**Learn more at:** www.med.upenn.edu/aging/events.html

## Make a Gift

To support aging-related research and care at Penn's Institute on Aging, contact:
**Elizabeth Yannes, Penn Medicine Development**
elyannes@upenn.edu or 215-573-4961

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