# New Grants Awarded For Alzheimer's Research

Each year, the NARFE-Alzheimer's National Committee determines which research projects will be awarded grants from the NARFE-Alzheimer's Research Fund.

NARFE has awarded a total of 89 research grants since the NARFE/Alzheimer's Partnership began in 1985. In fiscal year 2022, NARFE members donated $600,982 to the fund. Therefore, at NARFE Alzheimer's National Annual Training Meeting, held virtually October 20-21, the committee awarded four new grants totaling $600,982. This year's grants are awarded to:

**Emily Hokett, Ph.D.,** Columbia University (New York, NY), $175,000, fully funded over three years for her research on "Sleep and Psychosocial Factors Linked to Cognition in Alzheimer's Disease."

This study will look why older Black or African American individuals are twice as likely and Hispanic/Latino individuals are about 1.5 times as likely to develop dementia as older white individuals.

Black and Latino adults are at greater risk of experiencing poor quality sleep as compared to white adults. According to recent studies, it was revealed that sleep disruption may influence the risk for Alzheimer's and other brain diseases. It also revealed that more than 50% of individuals with dementia experience sleep disruptions or poor sleep patterns that precede cognitive impairment by several years. It is also believed that short sleep duration and poor sleep quality may be linked with Alzheimer's-related brain changes, to include the abnormal accumulation of beta-amyloid and tau protein, which are two hallmarks of Alzheimer's. Other studies have also linked poor sleep quality and sleep duration that is either too long or too short with poorer cognitive performance. Participants in these studies have been predominantly white, making the association between sleep and Alzheimer's in Black and Latino populations unknown.

This project may contribute to a better understanding of modifiable risk factors for Alzheimer's, such as poor sleep and other psychosocial factors. If this is successful, the findings might inform preventive strategies for Alzheimer's, especially for Black and Latino older adults.

**Jingjing Gao, Ph.D.,** Brigham and Women's Hospital (Boston, MA), $174,994, fully funded over three years for her research on ''RNAi Gene Therapy Targeting Microglial CD33 for Alzheimer's Disease."

This study will look at whether reducing the activity of protein on the surface of brain cells can prevent Alzheimer's-related brain changes.

Microglia are the brain's primary immune cells. They sense and help remove unwanted proteins from the brain in part through "phagocytosis," a process in which microglial cells engulf (or "swallow") the unwanted proteins. Research appears to have shown that microglia become impaired in Alzheimer's and may lose their ability to clear unwanted molecules and proteins through phagocytosis properly. This impairment may occur in part because a protein on the surface of microglia called CD33 becomes overly active and then inhibits several microglial functions, which includes phagocytosis. Recent studies have shown that mice genetically engineered to lack CD33 produce less beta-amyloid protein "plaques," a hallmark brain change research of Alzheimer's.

Scientists are now developing new methods to reduce levels of CD33 as a potential therapy for Alzheimer's. One method would involve injecting RNAi (RNA interference) molecules targeting the CD33 gene into the brain to possibly preventing it from making CD33 protein.

**Pinar Ayata, Ph.D.,** City University of New York (New York, NY) $150,000, fully funded over three years for her research on "Cellular Events That Shape Microglial Identity in Alzheimer's Disease."

This study will look at whether long-term changes in brain immune cells lead to nerve damage and Alzheimer's disease.

While the scientists do not seem to know exactly how

microglia becomes damaged in Alzheimer's, recent studies indicate that the process may involve several long-term genetic and molecular mechanisms. These mechanisms include protestasis, which is the ability of brain cells to replace unwanted proteins with new ones; mitochondrial metabolism, the ability of energy-generating compartments within cells to convert sugar into energy, and DNA methylation, which a process by which genetic material turns genes "on" and "off" during different phases of the body's development.

Ayata and her team will investigate how long-term mechanisms may interact to alter the structure and function of microglia and the relationship between microglia and brain diseases.

**Xu Hou, Ph.D.,** Mayo Clinic in Florida (Jacksonville, FL), $100,988 out of $140,000, partial funding over three years for her research on "APOE4-linked Mitophagy Change in Human Disease Brain and iPSC Models."

This study will look at how many specific gene variations promote disease-related damage to cell structures in the brain.

Mitochondria are specialized structures inside cells that function as the powerhouse of energy generation for the cells. Typically, mitochondria keep themselves healthy in part through "mitophagy," a process in which damaged mitochondria are identified and removed. Studies suggest mitophagy becomes dysfunctional early on in Alzheimer's and Lewy body dementia (LBD).

In the initial research, Hou and her colleagues examined mitophagy changes in genetically engineered Alzheimer's-like mice, in cells developed in a laboratory dish, and in brain samples from individuals who either has Alzheimer's or LBD. They found that these mitophagy changes were associated with a gene variation called APOE4, which has been shown to increase dementia risk in certain populations.

Hou's team will conduct a larger study to better understand the complex relationship of APOE4 and mitochondrial dysfunction in brain diseases. ■

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