American Heart Association.

THE PAUL G. ALLEN FRONTIERS GROUP

STRATEGIC FUNDING INITIATIVE

BRAIN HEALTH & COGNITIVE IMPAIRMENT

TOTAL INVESTMENT 2019–2026

MORE THAN $43 MILLION IN RESEARCH

BY THE NUMBERS

49 new grants in **30** research/disease categories, with more than **$50 Million** in subsequent funding from the NIH

49 publications directly attributable to BHCI PIs and **415** related pubs to date

5 patent applications have been filed from the BHCI researchers

NOTABLE PUBLICATIONS

Increased post-mitotic senescence in aged human neurons is a pathological feature of Alzheimer's disease, *Cell Stem Cell*, December 2022

The Salk team found that Alzheimer's disease (AD) brains have significantly higher proportions of neurons that express age-related biomarkers. Genomic testing on AD brain cells showed oncogenic challenges and metabolic dysfunction as well as signs of inflammation. The researchers show that targeting these neurons with specific therapeutics could be a strategy for preventing or treating AD.

A human brain vascular atlas reveals diverse mediators of Alzheimer's risk, *Nature*, February 2022

Stanford researchers developed techniques to profile the major vessel cell types in the human brain in patients with Alzheimer's disease (AD) and others with no cognitive impairment. For patients with AD, the researchers found vulnerabilities in the extracellular matrix (ECM) and signs of dysregulated blood flow. Their work uncovers the molecular basis of the human brain vasculature, which will inform our understanding of overall brain health, disease and therapy.

Reducing acetylated tau is neuroprotective in brain injury, *Cell*, April 2021

Traumatic brain injury (TBI) is a risk factor for Alzheimer's disease (AD). The University Hospitals team are identifying targets and potential blood biomarkers of TBI that could be therapeutic sites and might lead to reversal of TBI.

BHCI COLLABORATIVE GRANTS

Dr. Jeffrey Jones (Salk Institute) & Dr. Travis Conley (Stanford University)

Determination of the Role of Kynurenine in Models of Alzheimer's Disease

The goal is to understand how a by-product of metabolism might affect the way brain cells work together in mice with changes similar to Alzheimer's. They will use special techniques and drug intervention to determine if they can improve memory and the health of brain cells similar to those seen in Alzheimer's disease.

Dr. Courtney Glavis-Bloom (Salk Institute) and Dr. Patricia Moran Losada (Stanford University)

Proteomic Clocks of Cognition: Mapping Plasma Proteomic Signatures That Underlie Cognitive Aging in Non-human Primates

The researchers are working to help people age well by understanding biological reasons for changes in thinking and memory. The researchers are using a group of marmosets (small monkeys) from young to old age to determine how their thinking changes. They will then connect these cognitive changes with different molecules found in the marmosets' blood.

Dr. Nannan Lu (Stanford University) and Dr. Lara Labarta-Bajo (Salk Institute)

Regional Heterogeneity of Astrocyte and Microglia in the Uptake of Blood Factors During Aging and In ammation

The researchers are investigating if aging or inflammation worsens communication between the blood and brain cells and are hoping to identify specific blood proteins when bodies experience inflammation. Results from this proposal could be used to develop therapies that prevent unhealthy aging.