NIH Targets Links Between Vascular Disease and AD

Seeking a better understanding of vascular contributions to Alzheimer's disease (AD), the National Institutes of Health (NIH) announced on March 14 the launch of the Molecular Mechanisms of the Vascular Etiology of Alzheimer's Disease (M^2OVE-AD) Consortium, a team-science venture to build a nuanced model of AD that will more accurately reflect its many causes and pathways. Scientists have long been interested in the ways in which the vascular system may be involved in the onset and progression of AD and related dementias. Scientists from diverse fields will work collaboratively toward shared goals to dissect the complex molecular mechanisms by which vascular risk factors influence AD and identify new targets for treatment and prevention. Developed by the National Institute on Aging (NIA) and the National Institute of Neurological Disorders and Stroke (NINDS), the 5-year, $30-million program brings together more than a dozen research teams working on several complementary projects. Harnessing the power of new molecular technologies and big data analytics, the teams will make biological datasets available to the wider research community.

"Despite evidence that the brains of most AD patients have a variety of vascular lesions and that midlife diabetes and high blood pressure are major risk factors for AD, our understanding of the molecular mechanisms involved is quite limited," said NIA Director Richard J. Hodes, MD. "M^2OVE-AD will not only advance our understanding of these mechanisms but also identify the molecular signatures—sets of genes, proteins and metabolites—that may be used as markers for disease risk or to track the effectiveness of promising therapies."

The teams will generate several layers of molecular data from brain tissue donated by deceased AD research participants and from blood cells and plasma donated by living study participants with various types of vascular risk. Researchers will then develop mathematical models of the molecular processes that link vascular risk factors to AD onset and progression by combining molecular data with data on cognition, brain imaging, and several measures of vascular health. In parallel, the teams will use a number of animal models that show different vascular disease traits to elucidate the molecular mechanisms linking vascular risk factors and AD and to test predictions made from analyses of human data.

"A growing body of research suggests vascular damage often contributes to AD," said Roderick Corriveau, PhD, program director, NINDS. "This focused collaborative effort may push our understanding of AD over a tipping point and facilitate the development of better treatments for those who are suffering."

M^2OVE-AD builds on the open science approach and big data infrastructure established by the Accelerating Medicines Partnership–Alzheimer's Disease effort, a precompetitive partnership between NIH, industry, and nonprofit organizations to speed the discovery of promising therapeutic targets and disease biomarkers. "Breaking down the traditional barriers to collaboration and data sharing is key to moving the science forward, so we've ensured that the discoveries each team makes can be rapidly shared among the consortium and the wider research community," said Suzana Petanceska, PhD, senior advisor for strategic development and partnerships in the NIA Division of Neuroscience. "We've also established a panel of external leading experts to help shape the direction of M^2OVE-AD research and, potentially, bring about new partnerships and avenues of investigation."

Projects supported by M^2OVE-AD include:

Integrative Translational Discovery of Vascular Risk Factors in Aging and Dementia: Guojun Bu, PhD, and Nilufer Ertekin-Taner, MD, PhD, from the Mayo Clinic (Jacksonville, FL) in collaboration with researchers at Mayo Clinic (Rochester, MN) and the Icahn Institute for Genomics and Multiscale Biology (New York, NY), will investigate the ways in which molecular networks influence vascular risk in aging, AD, and other dementias.

Interdisciplinary Research to Understand the Interplay of Diabetes, Cerebrovascular Disease, and AD: José A. Luchsinger, MD, and Adam Brickman, PhD, from Columbia University (New York, NY), and Herman Moreno, MD, from SUNY Downstate Medical Center (Brooklyn, NY), will integrate studies in humans and in animal models to examine the interplay between diabetes, AD, and cerebrovascular disease.

The Role of the Renin Angiotensin–Endothelial Pathway in AD: Ihab Hajjar, MD, and Arshed Quyyumi, MD, from Emory University (Atlanta, GA), will focus on understanding the molecular mechanisms by which vascular dysfunction associated with high blood pressure affects the onset and progression of AD.

Metabolic Signatures Underlying Vascular Risk Factors for Alzheimer's-Type Dementias: Rima Kaddurah-Daouk, PhD, from Duke University (Durham, NC), and Mitch Kling, MD, from the University of Pennsylvania (Philadelphia), will lead a team to identify and define lipidomic signatures in plasma that are associated with cardiovascular disease and cognitive changes.

Cerebral Amyloid Angiopathy and Mechanisms of Brain Amyloid Accumulation: Steven Greenberg, MD, PhD, and Brian Bacskai, PhD, from Massachusetts General Hospital (Boston), will lead a team investigating the molecular mechanisms underlying cerebral amyloid angiopathy and its impact on AD.

Additional details on these funded projects are available at http://www.nih.gov/news-events/news-releases/decoding-molecular-ties-between-vascular-disease-alzheimers.

National Institutes of Health