An Innovative Approach to Study Alzheimer Disease Blood Biomarkers

https://neurodegenerationresearch.eu/survey/an-innovative-approach-to-study-alzheimer-disease-blood-biomarkers/

Principal Investigators

HU, BINGREN

Institution

UNIVERSITY OF MARYLAND BALTIMORE

Contact information of lead PI
Country

USA

Title of project or programme

An Innovative Approach to Study Alzheimer Disease Blood Biomarkers

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

388962.3853

Start date of award

01/04/2016

Total duration of award in years

1

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Biotechnology... Brain Disorders... Dementia... Neurodegenerative... Neurosciences... Prevention... Translational Research

Research Abstract

? DESCRIPTION (provided by applicant): Alzheimer’s disease (AD) is the public health crisis of the 21st century. Unless something is done, AD is projected to cost over $1.1 trillion by 2050, thus placing a huge burden on society (www.alz.org). At the diagnostic stage, AD pathologies are already quite advanced. Therefore, early (or pre-pathological) diagnostic biomarkers are

desperately needed. A hallmark of AD is significant accumulation of an array of AD-specific ubiquitinated proteins (ubi- proteins, e.g., ubi-APP) in brain tissue. This project will use a newl invented method to study early AD-related ubi-protein blood biomarkers. Methods of making antibodies against proteins post-translationally modified by a monomeric molecule, e.g., phosphorylated proteins, are already very well established. Phosphorylation site- specific antibodies have been widely used in acquiring knowledge, diagnosing disease, and developing therapeutic agents throughout the whole spectrum of life sciences. In comparison, there is no method currently available for making antibodies recognizing polymeric protein conjugates in a conjugation site-specific manner. Polymeric protein conjugation is defined as covalent conjugation between two polypeptides via amino acid side chains such as protein ubiquitination. Extensive efforts have been devoted to generating ubiquitin-to-protein conjugation site-specific antibodies, but without success. By using a state-of-the-art quantitative proteomic technology, we recently found that many ubi-protein conjugation site-specific peptide fragments are dramatically increased in brain samples from a transgenic AD mouse model at both early “”pre-pathological”” and “”advanced”” stages. We therefore employed a new method to make two ubiquitin conjugation site-specific antibodies for detecting potential blood biomarkers in a transgenic AD mouse model and an animal ischemia-reperfusion stroke model. We found that these ubi-protein conjugation site-specific epitopes were significantly increased in blood samples from the transgenic AD mice, but their levels were very low and basically unchanged in the blood samples from animals after middle cerebral artery occlusion (stroke model). This project will employ this new method to generate ubi-protein conjugation site-specific antibodies to study potential AD ubi- protein biomarkers in brain tissue and blood samples from two different transgenic mouse AD models. If the objectives of this proposal are achieved, these innovative approaches can be further applied to study new human AD biomarkers in brain tissue, CSF and blood samples. Therefore, the long-term objectives are to develop clinical assays of early human AD biomarkers for AD research, diagnosis and drug development.

Further information available at:

Types:
Investments < €500k

Member States:
United States of America

Diseases:
N/A

Years:
2016

Database Categories:
N/A

Database Tags:
N/A