Novel Multiplexing Proteomics to Study the Periphery in Alzheimers Disease

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Contact information of lead PI
Country

USA

Title of project or programme

Novel Multiplexing Proteomics to Study the Periphery in Alzheimers Disease

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,546,320.18

Start date of award

01/01/2016

Total duration of award in years

3

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Alzheimer's Disease, Proteomics, Oxidative Stress Pathway, Peripheral, Neuraxis

Research Abstract

? DESCRIPTION (provided by applicant): There is no cure for Alzheimer’s Disease (AD). Five million people nationwide are suffering from AD and this number will grow to 20 million as the

baby boomer generation continues to age. Even with current clinical and pathological knowledge about AD, the exact causes and factors that take place with disease progression are not fully understood. Interestingly, the liver generates toxic amyloid-? peptides that travel acros the blood brain barrier. Decreasing the liver's production of these peptides with drugs decreases brain amyloid-beta peptide levels in mice. Questions remain concerning how changes in the liver and other organs outside the central nervous system (CNS) influence onset, progression, and treatment of AD. Our laboratory has already shown that lipid and energy metabolism as well as oxidative stress pathways are altered in liver and peripheral T-cells in advanced stages of an AD mouse model. These changes may be connected to similar dyshomeostasis of these pathways that are well known to occur in the CNS. In order to gain a better understanding of AD, it is necessary to study changes outside of the CNS and fully understand how they relate to CNS. The PI's long-term objectives are to provide better information about molecular changes that initiate disease onset in AD and use this information to help facilitate new avenues for AD therapeutics. Quantitative proteomics is a powerful tool to apply to this problem because it tells us about changes in specific cellular functions. However, it is currently not possible to multiplex to the degree necessary for answering questions about the role of peripheral organs in AD. Here, we propose three aims to address this issue: Aim 1. Develop multiplexing capabilities to measure relative protein expression quantitatively in an unprecedented 60 tissue samples. Aim 2. Create selective multiplexing proteomics for post-translational modification of cysteine-containing proteins to understand the impact of oxidative stress on proteins in tissue. Aim 3. Elucidate AD pathogenesis in peripheral tissues for the first time to multiple peripheral organs (liver, heart, kidney, lung, and brain) from AD mice and age/sex-matched controls at ages before and after the onset of disease symptoms. These proteomics measurements will establish how altered metabolic- and oxidative-stress pathways in the periphery relate to changes in the CNS. Furthermore, the timing of these changes with disease onset and progression will be established. Successful completion of these aims will help to delineate how peripheral organs contribute to AD pathology and help facilitate new avenues for AD therapeutics. This outcome is necessary to further the mission of the NIH “”to conduct research in the causes, diagnosis, prevention, and cure of human diseases””.

Lay Summary
PUBLIC HEALTH RELEVANCE: There is no cure for Alzheimer's Disease (AD). Five million people nationwide are suffering from AD and this number will grow to 15 million in the next thirty years. This research will help facilitate new avenues for therapeutics by studying molecular changes in major organs and how they are related to changes in the AD brain.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:

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