Discovery of Novel Proteomic Targets for Treatment of Alzheimers Disease

https://neurodegenerationresearch.eu/survey/discovery-of-novel-proteomic-targets-for-treatment-of-alzheimers-disease-2/

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Country

USA

Title of project or programme

Discovery of Novel Proteomic Targets for Treatment of Alzheimers Disease

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 7,563,392.66

Start date of award

15/08/2014

Total duration of award in years

3

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

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

Research Abstract

DESCRIPTION (provided by applicant): This proposal uses proteomics to better understand Alzheimer’s disease pathogenesis with a large-scale, unbiased, and direct approach to discover and validate novel disease processes in postmortem AD brain, and to prioritize new targets for early stage therapeutic intervention. The AD proteome mediates the effects of aging, genetics and other risk factors and contains unidentified protein targets for therapies. The approach leverages the strengths of a national team of collaborating AD Centers and associated studies of aging, an innovative proteomics platform, advanced systems biology, and model systems to produce new treatment targets. The first aim will identify novel proteomic targets selectively altered in asymptomatic AD brain. Brains will be analyzed by mass spectrometry (MS), yielding discovery proteomes to compare 1) controls free of AD and other pathologies; 2) asymptomatic controls with AD pathology; 3) non-demented mildly impaired cases with AD pathology, 4) definite AD, and 5) other neurodegenerative diseases. Protein changes in synapses, insoluble aggregates, glial and neuron-specific nuclei, and select posttranslational modifications will be determined. Bioinformatics will be used with available large-scale data to identify potentially druggable targets in key networks and cellular processes. The second aim will validate candidate proteomic targets in postmortem brains from independent community and clinic-based cohorts and determine relationships with clinicopathological features, including cognition. Absolute levels of candidate proteins will be quantified using selected reaction monitoring MS. The third aim will establish links between the validated proteome and AD pathogenesis and druggability. The most promising candidates will be studied for effects on neuronal viability and interactions with Ass and tau using cell culture and drosophila models. These results and other data will drive selection of the most promising candidates to advance to mouse models to assess therapeutic potential.

Lay Summary

PUBLIC HEALTH RELEVANCE: Alzheimer’s disease (AD) is a devastating, common, and growing epidemic without an effective means of prevention or disease-modifying treatment. The proposal will discover and validate novel underlying mechanisms that trigger, resist, and/or promulgate the disease process, and identify promising new protein targets for effective treatments.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

Database Tags:
N/A