Identifying, validating and targeting AD susceptibility networks in monocytes

https://www.neurodegenerationresearch.eu/survey/identifying-validating-and-targeting-ad-susceptibility-networks-in-monocytes/

Principal Investigators

DE JAGER, PHILIP L

Institution

BRIGHAM AND WOMEN'S HOSPITAL

Contact information of lead PI
Country

USA

Title of project or programme

Identifying, validating and targeting AD susceptibility networks in monocytes

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,753,863.30

Start date of award

30/09/2014

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)... Brain Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Genetics... Immune System... Neurodegenerative... Neurosciences... Prevention

Research Abstract

DESCRIPTION (provided by applicant): Alzheimer's disease (AD) is an age-related neurodegenerative disease characterized by progressive cognitive decline and dementia as well as pre-symptomatic accumulation of amyloid pathology. A number of recently identified AD susceptibility loci contain genes expressed predominantly in myeloid cells, such as monocytes, macrophages and microglia. This suggests the involvement of the innate immune system in AD susceptibility and the accumulation of amyloid pathology. Therefore, we hypothesized that monocyte-derived cells, such as infiltrating macrophages as well as resident microglia are involved in the pathophysiology of AD and, particularly, in the accumulation of amyloid pathology. Our preliminary cis-eQTL analyses of data from healthy young individuals have implicated 16 AD susceptibility genes in myeloid cell function, whose expression, relative to each risk allele, is altered in monocytes and not in T cells that represent the adaptive arm of the immune system. Therefore, these loci represent excellent candidates as the first step in the cascade of molecular events that link genetic risk factors to the altered innate immune function that contributes to AD pathology. The principal goals of the proposed project are (1) to identify and validate the component genes of networks perturbed by the AD susceptibility loci in myeloid cells (2) to understand their functional consequences on monocyte behavior and (3) identify FDA- approved or novel small molecules that modulate the most promising targets for AD therapy in primary human monocytes.

Lay Summary
PUBLIC HEALTH RELEVANCE: Alzheimer's disease (AD) is an age-related neurodegenerative disease involving cognitive decline and dementia, and recent studies show that immune system dysfunction plays an important role in AD. Here, we identify and confirm the molecules that contribute to immune cell malfunction in AD, and we identify the FDA-approved or new drugs that reverse the effect of these molecules and restore the function of the affected immune cells.

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