Demystifying Microglia in Aging and Alzheimers Disease

https://www.neurodegenerationresearch.eu/survey/demystifying-microglia-in-aging-and-alzheimers-disease/

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Country

USA

Title of project or programme

Demystifying Microglia in Aging and Alzheimers Disease

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 3,695,800.00

Start date of award

01/09/2016

Total duration of award in years

1

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... Dementia... Genetics... Human Genome... Neurodegenerative... Neurosciences

Research Abstract

Inflammation has become a well-recognized component of most neurodegenerative disorders,

including Alzheimer’s disease (AD). Until recently, we did not have the tools to reliably separate resident brain microglia from peripheral myeloid cells to delineate their functions in the brain. In this proposal, we will characterize different myeloid cell populations, such as resident brain microglia and peripheral monocytes, using elegant single-cell next-generation RNA sequencing (scRNA-Seq). We will determine the response of these neural immune components to physiological brain activity and neurodegeneration. Using novel models of mice with conditional targeting, we will manipulate AD risk genes specifically in brain microglia, and characterize the consequences, at both the single-cell and whole-animal level, in wildtype mice and mouse models of AD-like pathology. Importantly, we will compare these gene expression profiles to those obtained from over 500 well- studied healthy individuals and AD patients to assess the relevance of different monocyte phenotypes to the onset and progression of human AD.

Lay Summary
Our findings, combined with those of recent genome-wide association (GWAS) and gene expression studies in human Alzheimer’s disease (AD), have revealed a striking preponderance of microglial and monocyte- associated genes. However, the molecular delineations of different monocyte populations in the brain, which include microglia, as well as the potential for functional subpopulations within these cell types that impact both pathology, as well normal brain function and aging, are unclear. To address these issues, we will conduct single-cell RNA sequencing (scRNA-Seq) in monocyte cells from the brains of wildtype and mouse AD model mice, as well as from mice carrying microglia-specific gene deletions, and compare these profiles to RNA-Seq data obtained from the brains of hundreds of human subjects to allow to evaluate, in a systematic and integrative way, the role of monocyte cells in both normal brain function and aging, as well as in the progression of age-related neurodegeneration, in both the mouse and the human.

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