Role of the Innate Immune System in Aging and Development of Alzheimers Disease

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Country

USA

Title of project or programme

Role of the Innate Immune System in Aging and Development of Alzheimers Disease

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5

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... Immune System... Neurodegenerative... Neurosciences

Research Abstract

DESCRIPTION (provided by applicant): A major health problem relates to progressive cognitive decline with age and the threat of Alzheimer's disease (AD). We postulate, based on provocative new data, that the brain's innate immune system plays a central role in successful aging and resistance to AD. The role of the innate immune system in aging and AD has received limited study and is poorly understood. This is due in part to confusion regarding microglial cells and how they relate to the peripheral inate immune system. We discovered unique biomarkers and microRNA/gene signatures for resident microglia in the brain vs. recruited monocytes in both mice and humans. This advance presents a unique opportunity to determine the functions and dysfunctions of innate immune cells in brain aging and the development of AD. Hypothesis to be tested: We hypothesize that changes in the innate immune system with age play a major role in the development of diseases of aging that affect the human brain, including AD. We have termed this the ""Innate immunity hypothesis of brain aging."" If our hypothesis is correct, it will change our understanding of the functions of microgli and macrophages in healthy aging and in AD and provide new therapeutic opportunities to treat AD by targeting these unique cell populations. We have established a comprehensive research strategy to test the key components of our hypothesis both in animal models and in aging human subjects. Aim 1. Investigate resident microglia/recruited macrophages in aging and AD mouse models. Using our unique markers that distinguish resident microglia from infiltrating monocytes, we will determine the gene/microRNA profiles of these two populations during aging and AD progression and study their interaction with A? oligomers. Aim 2. Target microglia and recruited monocytes as a treatment for AD in animal models. We will target cells of the innate immune system to treat animal models of AD based on our characterization of these cells. We will utilize our unique antibodies to microglia/ monocytes, antigomirs to unique microRNAs, and ligands of the TAM system. Aim 3. Investigate brain- resident microglia and monocytes during human aging and in AD. We will study two unique human cohorts. 1. We will investigate pathologic specimens from an aging brain cohort in collaboration with David Bennett (Rush Memory and Aging Project). We will perform immunopathological characterization of microglia and recruited monocytes in healthy aged brains and those with typical AD and correlate changes in microglia with changes that occur in aging. 2. We will investigate the relationship between A? deposition in the brains of an aging human population (measured by PiB imaging) and the innate immune system in the peripheral blood. We will characterize monocytes in the blood from an aging cohort (under NIH study by Dr. Reisa Sperling at Brigham and Women's Hospital) in whom PiB imaging and cognitive assessment is being performed. This will provide a direct link between the peripheral innate immune system and brain changes with aging.

Lay Summary
There is decrease in brain function with aging that leads to cognitive decline and in some instances Alzheimer's Disease (AD). We hypothesize that the innate immune system plays a major role in aging and the development of AD. We will study this relationship to develop treatments to prevent AD and cognitive decline with aging.

Further information available at:

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Investments > €500k

Member States:
United States of America

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Alzheimer's disease & other dementias

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2016

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