Early detection of Alzheimers (MCI stage): Analysis of plasma cell-free miRNA

https://www.neurodegenerationresearch.eu/survey/early-detection-of-alzheimers-mci-stage-analysis-of-plasma-cell-free-mirna/

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Early detection of Alzheimers (MCI stage): Analysis of plasma cell-free miRNA

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NIH (NIA)

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01/07/2013

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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... Clinical Research... Clinical Research - Extramural... Clinical Trials and Supportive Activities... Dementia... Neurodegenerative... Neurosciences... Prevention... Translational Research

Research Abstract

DESCRIPTION (provided by applicant): Alzheimer's disease (AD) is the most common neurodegenerative disease (ND). Currently in the US there are 5.4M AD patients; associated healthcare cost is $200B per year. 10-20% of people age 65+ have Mild Cognitive Impairment (MCI) of which estimated 15% progress to dementia annually. Although no disease- modifying therapy for AD is available, stratified analysis of data from recent clinical trials revealed promising results for early stage patients. Thus, there is a great need for accurate noninvasive cost-effective diagnostics for primary screening. DiamiR develops innovative tests for early detection and monitoring of AD and other NDs based on analysis of brain-enriched microRNAs (miRNAs) circulating in plasma. Recently we identified and validated a biomarker signature of 6 miRNA pairs ("''miR-132?" and "''miR-134?" families) capable of differentiating MCI from age-matched control with up to 96% accuracy. In the SBIR Phase I study several additional miRNA pairs have shown promise for prediction of MCI to AD transition and differentiation of MCI and AD from Parkinson's disease (PD). The present SBIR Phase II study aims to test candidate miRNA biomarkers identified at DiamiR in plasma samples from larger, well-characterized, heterogeneous cohorts of patients from both prospective and retrospective studies, so as to validate biomarker miRNA signatures for early specific detection of AD. Specific aims include determining how early MCI and AD can be detected, and whether progression from pre-MCI and MCI to AD can be reliably predicted; assessing correlation of the miRNA biomarkers with existing biomarkers of AD (neuroimaging and cerebrospinal fluid biomarkers); and validation of biomarker miRNA signatures for differentiation of AD from other NDs – PD, Frontotemporal Lobe Dementia (FTLD), and Amyotrophic Lateral Sclerosis (ALS). The hypothesis underlying DiamiR's approach to biomarker discovery is as follows: since early stages of NDs are characterized by neurite and synapse destruction in distinct brain areas and neuron types, we hypothesize that miRNA biomarkers for detection of early stages of AD, prediction of pre-MCI and MCI progression to dementia, and differentiation of AD from other NDs can be defined using biomarker miRNA pairs, with each pair consisting of (1) miRNAs which are enriched in brain regions affected by a pathology (hippocampus for AD, midbrain for PD, motor neurons for ALS, etc.) and also present in neurites and synapses; and (2) other brain-enriched miRNAs present in cells and brain regions not involved in the pathology, used as normalizers, so as to compensate for factors not re- lated to the pathology. Additional potentially useful miRNA pairs consist of miRNAs not enriched in the brain, but involved in the processes characteristic of progressive disease stages (e.g. inflammation, apoptosis); and of brain-enriched miRNAs. Lab-Developed Tests (LDTs) based on the miRNA signatures validated herein will be developed under CLIA guidelines and used to screen patients for clinical trials. The tests will assist researchers and clinicians with detecting MCI and predicting whether MCI will progress to AD or other NDs.

Lay Summary
PUBLIC HEALTH RELEVANCE: In this Phase II SBIR DiamiR plans to examine blood samples from a large number of patients to confirm the utility of novel blood-based biomarkers for early, specific detection of Alzheimer's disease. The biomarkers, previously identified at DiamiR, are pairs of certain microRNA molecules, which are present in different regions of the brain, and are also detectable in blood. Diagnostic tests based on the validated biomarkers will be used to screen asymptomatic and early stage patients for clinical trials aimed at prevention of Alzheimer's dementia.

Further information available at:

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Investments > €500k

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United States of America

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Alzheimer's disease & other dementias

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2016

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