Genomic and Metabolomic Data Integration in a Longitudinal Cohort at Risk for Alzheimers Disease

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Principal Investigators

ENGELMAN, CORINNE D.

Institution

UNIVERSITY OF WISCONSIN-MADISON

Contact information of lead PI
Country

USA

Title of project or programme

Genomic and Metabolomic Data Integration in a Longitudinal Cohort at Risk for Alzheimers Disease

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NIH (NIA)

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15/08/2016

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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)... Biomedical Information Resources...

Biomedical Information Resources and Informatics Research... Biotechnology... Brain Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Genetics... Human Genome... Neurodegenerative... Neurosciences... Precision Medicine... Prevention

Research Abstract

PROJECT SUMMARY A longitudinal multi-omics examination of ?-amyloid (A?) deposition, cognitive decline, and resilience in the years prior to Alzheimer's disease (AD) diagnosis is critical to better understand, prevent, diagnose, and treat the disease. Common genetic variants in APOE and 19 additional genes have been associated with AD. Low frequency and rare functional variants with moderate effects on risk for AD have recently been identified through sequencing studies, with additional variants remaining to be discovered. Metabolic profiles, which reflect the combined effect of genes, intrinsic metabolism, environmental exposure, and interactions between these, have also been associated with AD. However, the cause of AD is not well understood and there are currently no effective preventions or treatments for this common disease. Integration of genomic and metabolomic data will enable thorough and comprehensive modeling and identification of the complex interplay of genes and metabolites involved in AD pathology. Continuing to focus on single-data-type study designs, which do not accurately reflect the complexity of AD, will hinder progress in our understanding of this disease and of effective prevention, diagnosis, and treatment. Our long-term goal is to elucidate complex interactions involved in AD pathology using a comprehensive set of omics data in order to inform precision medicine for AD. The objective of this proposal is to define the role of genomics and metabolomics in A? deposition, cognitive decline, and resilience in initially asymptomatic participants with a parental history of AD diagnosed by age 75, with replication in an existing independent cohort. The specific aims are to use genomic sequencing and metabolomics to identify 1) common and rare genetic variants, 2) metabolic profiles, and 3) complex interactions between genomics and metabolomics that are involved in AD, A? deposition, cognitive decline, and cognitive resilience. A sample of 344 eligible participants, aged 40-65 at baseline, have been identified from the longitudinal Wisconsin Registry for Alzheimer's Prevention (WRAP) and ~506 extended family members of these participants will also be enrolled. Participants from the longitudinal Wisconsin-Alzheimer's Disease Research Center (W-ADRC) will be used for replication.

Lay Summary

PROJECT NARRATIVE The rationale for our proposed research is that integration of genomic and metabolomic data will enable modeling and identification of the complex interplay of genes and metabolites involved in AD pathology, which is necessary to achieve the goal of precision medicine for AD. This contribution will be significant because identification of novel genes, metabolic profiles, and interactions between the two is expected to lead to: identification of new pathways to target with therapeutic agents; novel risk prediction and diagnostic tools for early AD pathophysiology; and dietary, lifestyle, or environmental interventions to prevent or impede AD.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

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N/A

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