Sequence-based Discovery of AD Risk & Protective Alleles

https://neurodegenerationresearch.eu/survey/sequence-based-discovery-of-ad-risk-protective-alleles/

Principal Investigators

WIJSMAN, ELLEN M

Institution

UNIVERSITY OF WASHINGTON

Contact information of lead PI
Country

USA

Title of project or programme

Sequence-based Discovery of AD Risk & Protective Alleles

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 2,619,832.11

Start date of award

15/06/2014

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)... Biotechnology... Brain Disorders... Dementia... Epidemiology And Longitudinal Studies... Genetics... Human Genome... Minority Health for IC Use... Neurodegenerative... Neurosciences... Prevention

Research Abstract

DESCRIPTION (provided by applicant): This Sequence Analysis Consortium (SAC) brings together experts in Alzheimer’s disease (AD), human genetics, biostatistics and genome sciences to identify risk and protective single nucleotide and copy number variants (SNVs and CNVs) influencing AD and AD-related endophenotypes. This SAC will harmonize and integrate genomic and phenotype data (generated by Core C) from the AD Sequencing Project (ADSP) and other data resources and use the most informative analytic methods (as determined by Core B) to identify novel risk and protective alleles. This SAC is partially based on the ADSP case-control study design with whole exome sequencing in 6,888 cases who developed AD despite an ‘a priori low risk’ and are likely enriched for novel risk variants, and 14,400 cognitivly normal older controls, a subset of whom are enriched for protective variants. To allow novel discovery in minority populations that carry a disproportionate burden of AD, we will analyze exome sequence data and well-characterized endophenotypes, including verbal memory and hippocampal volume (harmonized by Core D). Replication will be afforded using targeted sequence and genotype data in 50,000 cases and controls and 40,000 individuals with endophenotype data. We will seek to identify SNVs (Project 1) and CNVs (Project 2) contributing to AD susceptibility and protection. Integrated and annotated (using ENCODE and the Epigenomic Roadmap Projects) SNVs and CNVs data from the ADSP families with whole genome sequencing, as well as other familial AD resources will be used for genetic linkage and IBD analyses (Project 3) to identify AD susceptibility or protective alleles in highly-ascertained, multiplex families. The case-control design (Projects 1 and 2) and the family design (Project 3) complement each other to maximize discovery of AD variants. In order to promote AD translational research and discovery, we will collaborate with other researchers to undertake further replication and functional studies, create public resources with integrated genomic and phenotypic data, and make available computational algorithms through the public domain. Identification of variants in genes leading to risk and protection from AD may ultimately lead to novel treatments and prevention strategies.

Lay Summary

PUBLIC HEALTH RELEVANCE: Alzheimer’s disease is a common disease of aging characterized by loss of memory, and Alzheimer’s disease clusters in families. This Project seeks to identify genes associated with increased risk of Alzheimer’s Disease or protection from it. This newly discovered genetic information may help to identify novel treatments for this debilitating condition.

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

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