Search for the Alzheimers Genes

https://www.neurodegenerationresearch.eu/survey/search-for-the-alzheimers-genes/

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Country

USA

Title of project or programme

Search for the Alzheimers Genes

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 3,645,278.90

Start date of award

01/07/2007

Total duration of award in years

7

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

Research Abstract

? DESCRIPTION (provided by applicant): This competitive renewal application seeks to continue a project on the genetics of Alzheimer’s disease (AD). As part of the funded project we

performed genome-wide association study (GWAS) on our case-control sample that has contributed to the identification of multiple novel loci for AD as part of national and internationl collaborations. In addition to GWASs, we also performed several association studies on candidate genes that resulted in >50 publications during the current grant period. Confirmed loci identified for AD risk using the case-control association design account for only ~30% of the phenotypic variance. An alternative approach focusing on AD quantitative phenotypes/endophenotypes may help to identify additional genes for AD, as this approach can be more powerful than using the binary case-control design. As part of our preliminary data for this renewal, we have completed GWASs on four AD-related phenotypes: deposition of Aß in the brain measured by amyloid imaging, short-term disease progression measured by change in Mini-Mental State Examination (MMSE) score over 12 months, disease progression measured by time to reach MMSE 9 score (indicator of moderate to severe AD), and survival time in AD. We have identified novel loci for each AD- related phenotype. Using pathway analysis we have also identified multiple potentially novel candidate genes in the networks of GWAS-implicated genes. Since GWAS arrays use an indirect approach that relies on linkage disequilibrium to detect association signals, rarely are the identified significant variants the causal variants. Thu, it is important to resequence the candidate gene regions implicated by GWASs and those that participate in their networks in order to characterize the full spectrum of common, low-frequency and rare causal variants associated with AD-related phenotypes. The objective of this renewal application is to perform targeted resequencing of selected top gene regions implicated by GWASs and additional candidate genes in the networks of GWAS-implicated genes in order to identify causal variants associated with four AD-related phenotypes. Replication of significant variants obtained in the discovery stage will be sought in independent sets of replication samples. Finally, we will examine the functional nature of the identified significant variants usin bioinformatics tools and brain gene expression data. The successful completion of the proposed comprehensive studies will likely lead to the identification of new AD-related genes/variants.

Lay Summary

PUBLIC HEALTH RELEVANCE: Alzheimer’s disease (AD) is a major public health problem. Currently there is no effective treatment for AD. In this renewal we focus on the genetics of AD-related phenotypes that will likely lead to the identification of new genes/variants that are relevant to AD. Our novel preliminary genetic data on AD progression and survival support the notion that there are sub-groups of AD patients and the precise identification of genetic factors, as part of this proposal, may help in predicting the progress of disease and assignment of patients to tailored drug treatment.

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