Identification and characterization of AD risk networks using multi-dimensional omics data

https://www.neurodegenerationresearch.eu/survey/identification-and-characterization-of-ad-risk-networks-using-multi-dimensional-omics-data/

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Country

USA

Title of project or programme

Identification and characterization of AD risk networks using multi-dimensional omics data

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 3,781,156.88

Start date of award

15/07/2016

Total duration of award in years

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)... Biotechnology... Brain Disorders... Dementia... Genetics... Human Genome... Neurodegenerative... Prevention... Translational Research

Research Abstract

? DESCRIPTION (provided by applicant): Genome-wide association, whole genome/exome sequencing and gene network studies have already enabled researchers to identify twenty loci influencing Alzheimer’s disease (AD) risk and another half dozen genes carrying specific rare variants that influence disease risk. With the new whole-genome sequence (WGS) and whole-exome sequence (WES) data from 10,000+ AD cases and controls from the ADSP, combined with mRNA expression data from 3,500+ individuals from AMP, it is now possible to develop a more comprehensive picture of the genetic architecture of AD and associated risk. Beyond refining AD genetic architecture, our goal is to identify and validate therapeutic targets for AD b identifying genes that functionally drive or protect from AD and interrogating their respective gene networks for therapeutic targets. We will do this using the largest, most comprehensive data set, to date. Genetic and pathway-based analyses have strongly implicated a small number of networks including immune response, phagocytosis, lipid metabolism and endocytosis. We will integrate data from genetic studies and gene expression/regulation studies to identify risk and resilience genes to pinpoint key networks that functionally drive AD development and progression. We will take two complementary approaches to identify risk and resilience AD genes: (1) we will use a family-based approach to identify both risk and protective alleles using publicly available data and our own WGS/WES data from both NIALOAD and Utah families; and (2) we will use publicly available high-dimensional molecular data from AD cases and controls to construct global interaction and causal networks. We will then focus our analysis of ADSP case control sequence data on the most compelling networks, thereby reducing our search space and increasing power. To identify therapeutic targets, we will use network analysis to test known drugs that target networks identified in our sequence analysis of both family-based and case control data. We will then validate our findings by performing in vitro experiments based our in silico observations and determine the functional consequences of risk/resilience alleles identified from the AD sequence data. Together, the findings from this study will pinpoint key networks that functionally drive AD and will provide critical insight into therapeutic intervention

Lay Summary

PUBLIC HEALTH RELEVANCE: Alzheimer’s disease (AD) is the most common form of dementia but has no effective prevention or treatment. Developing a comprehensive picture of the genetic architecture of AD including a network level assessment of risk/resilience genes is essential to develop novel therapeutic targets. The goal of this study is to define molecular networks enriched for AD risk/resilience genes and to identify known drugs that influence these networks. Finally we will experimentally validate the top in silico predictions of implicated networks, genetic variation and candidate drugs.

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