Higher Order Chromatin and Genetic Risk for Alzheimers Disease

https://neurodegenerationresearch.eu/survey/higher-order-chromatin-and-genetic-risk-for-alzheimers-disease/

Principal Investigators

ROUSSOS, PANAGIOTIS

Institution

ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI

Contact information of lead PI
Country

USA

Title of project or programme

Higher Order Chromatin and Genetic Risk for Alzheimers Disease

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 2,887,195.41

Start date of award

01/09/2015

Total duration of award in years

2

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... Dementia... Genetics... Human Genome... Neurodegenerative... Neurosciences... Prevention

Research Abstract

? DESCRIPTION (provided by applicant): The genetics of Alzheimer’s Dementia (AD) is

advancing at rapid pace. An increasing number of risk- associated polymorphisms and variants are found in intergenic, intronic and other non-coding sequence. However, it has been a major challenge to design testable hypotheses to elucidate the potential function of such types of disease-associated non-coding DNA. Many of these sequences are thought to exert regulatory functions, including longe range enhancer elements physically interacting with transcription start sites (TSS) separated on the linear genome by many kilobases of interspersed DNA. We will first generate a comprehensive annotation map of open chromatin and enhancer sequences in tissue and cellular populations (neurons, astrocytes and microglia) that are relevant to the pathophysiology of AD. We will then leverage high resolution expression quantitative trait loci (eQTL) maps from two large, multiregional RNAseq projects in brain tissue and identify AD associated noncoding regions that are positioned within regulatory regions tagged with combinatorial histone modification signatures indicative of active enhancers and statistical (eQTL) evidence for long range TSS interactions. We then will employ innovative approaches in neuroepigenetics, including chromosome conformation capture (3C) to map long range enhancer-promoter interactions in human brain postmortem tissue. The multidimensional approach presented here provides a roadmap to unravel the neurological functions of the vast but in brain largely unexplored non-coding sequences of the human genome.

Lay Summary
PUBLIC HEALTH RELEVANCE: Alzheimer’s disease (AD) affects half the US population over the age of 85 and the costs are staggering in human and financial terms. We will study the chromosomal loopings and other three-dimensional higher order chromatin at risk-associated DNA variants and polymorphisms in human brain tissue. These data will provide first insights into the role of non-coding DNA for spatial genome architecture in human brain cells, including potential alterations in AD.

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