Using genetic variability in whole transcriptome expression in cells and tissues to understand the pathogenesis of Parkinson's and Alzheimer's disease

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Contact information of lead PI
Country

United Kingdom

Title of project or programme

Using genetic variability in whole transcriptome expression in cells and tissues to understand the pathogenesis of Parkinson's and Alzheimer's disease

Source of funding information

MRC

Total sum awarded (Euro)

€ 1,448,361

Start date of award

01/05/2013

Total duration of award in years

3.0

The project/programme is most relevant to:

Alzheimer's disease & other dementias|Parkinson's disease & PD-related disorders

Keywords
Research Abstract

The aim of this study is to determine the effect of genetic risk factors on whole transcriptome expression in brain regions and cell types most vulnerable to Parkinson's and Alzheimer's disease (PD and AD) in order to understand the pathogenic processes underlying these conditions. This project is inspired by the recent discovery of 15 new genetic risk variants for PD and 13 new loci for AD. However, knowing the genomic position of risk variants is not equivalent to knowing how they act in terms of the underlying molecular processes or where they act in terms of the regional or cellular location. We aim to address both these issues. Using control post-mortem human brain tissue originating from 150 individuals, we will use expression quantitative trait locus (eQTL) mapping and allele-specific expression (ASE) analysis to identify loci that both change disease risk and regulate the expression of specific gene transcripts within specific tissues/cells. We will conduct these studies within the tissues and cells most relevant to PD and AD, namely the substantia nigra, hippocampus, temporal cortex, dopaminergic neurons, CA1 neurons, pyramidal neurons and astrocytes. Existing exome sequencing and SNP array data will be combined with whole transcriptome RNA sequencing data generated on the Illumina HiSeq2000 platform for downstream analysis. These two types of information – genetic variation and transcript expression – will be used for eQTL mapping in tissues and ASE analysis in cells. In both cases the eQTLs identified will be annotated for disease-relevance in the first instance. All the data generated by this project will be publicly released as both raw data files for re-analysis and processed information suitable for non-expert users through NCBI's Gene Expression Omnibus repository and Phenotype-Genotype Integrator sites. Thus, we will generate novel disease-relevant findings and provide the neuroscience community with a world-class resource.

Lay Summary
Further information available at:

Types:
Investments > €500k

Member States:
United Kingdom

Diseases:
Alzheimer's disease & other dementias, Parkinson's disease & PD-related disorders

Years:
2016

Database Categories:
N/A

Database Tags:
N/A