Influence of genotype on microglia phenotype and function in PD

https://www.neurodegenerationresearch.eu/survey/influence-of-genotype-on-microglia-phenotype-and-function-in-pd/

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Contact information of lead PI
Country

USA

Title of project or programme

Influence of genotype on microglia phenotype and function in PD

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 1,300,354.13

Start date of award

01/09/2015

Total duration of award in years

3

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Microglia, Parkinson Disease, Genotype, Disease susceptibility, innate immune function

Research Abstract

? DESCRIPTION (provided by applicant): Parkinson’s disease (PD) is a degenerative disease of the central nervous system (CNS) characterized by the accumulation and aggregation of a-

synuclein in which the dopaminergic neurons of the substantia nigra die. The innate immune system is thought to play a role in the demise of these neurons. Therefore, we hypothesized that genotypic differences in microglia are involved in the pathophysiology of PD and, particularly, in the death of these dopamine producing cells. Our preliminary cis-eQTL analyses of data from healthy young individuals have implicated 11 PD susceptibility genes in myeloid cell function, whose expression, relative to each risk allele, is altered in the innate immune cell type monocytes and not in T cells that represent the adaptive arm of the immune system. Therefore, these loci represent excellent candidates as the first step in the cascade of molecular events that link genetic risk factors to the altered innate immune function that contributes to PD pathology. The principal goals of the proposed project are (1) to identify the component genes of networks perturbed by the PD susceptibility loci in myeloid cells (2) to understand their functional consequences on microglia behavior and (3) examine the role of these susceptibility loci on CNS microglia activation and gene expression.

Lay Summary
PUBLIC HEALTH RELEVANCE:: Influence of genotype on microglia phenotype and function in PD Project Narrative Relevance to public health. This project is of direct relevance to Parkinson’s disease, as we are proposing to study the discovery of novel targets associated with genetic variants expressed in the innate immune system that lead to Parkinson’s disease. We are examining monocyte-derived microglia-like cells from patients with Parkinson’s disease, as well as healthy young subjects to examine the genetic variation with-out the confounder of disease. We will use a systems biology approach to unravel the complexity of genome-wide association studies and identify key nodes in the networks that could serve as therapeutic targets. Our data will potentially provide a therapy to target the innate immune system contribution to Parkinson’s disease.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Parkinson's disease & PD-related disorders

Years:
2016

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