Understanding the pathological pathways to Parkinson's

https://neurodegenerationresearch.eu/survey/understanding-the-pathological-pathways-to-parkinsons/

Principal Investigators

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Country**

United Kingdom

Title of project or programme

Understanding the pathological pathways to Parkinson's

Source of funding information

Parkinson's UK

Total sum awarded (Euro)

€ 6,779,000

Start date of award

01/02/2010

Total duration of award in years

6.0

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

**Keywords
Research Abstract**
The Oxford Parkinson's Disease Consortium (OPDC) will use the unique interdisciplinary research environment within Oxford to establish a leading centre focussed on understanding the earliest pathological pathways in PD. Internationally-recognised scientists with strengths in genetics and genomics, transgenic rodent models, in vivo neuroanatomy and neuropharmacology of the basal ganglia, magnetic resonance imaging (MRI), and analysis of

protein biomarkers, will work closely with experts in the clinical epidemiology and clinical neurology of Parkinson's.

We will identify putative causal genetic variants within pathways leading to Parkinson's from bioinformatics analyses of large-scale genomics projects. Variants will be further characterised by resequencing genes in a large clinical cohort of 1700 Parkinson's patients and 300 aged-matched controls. Induced pluripotent stem cells generated from individuals harbouring susceptibility variants will be differentiated into dopaminergic neurons. The effects of genetic variants on genome-wide transcription and cellular dopamine homeostasis in cultured neurons will identify the best candidates to use in improved rodent models. BAC-transgenesis will be used to express causal variants at physiologically-relevant levels preserving temporal and spatial expression.

These new models will be analysed for the earliest changes of dopamine neuropharmacology, basal ganglia circuitry and neuropathology, and compared to high-resolution MRI of the midbrain of individuals from the OPDC clinical cohort with Parkinson's or at high risk for Parkinson's. Biomarker studies on microRNAs and proteins will correlate peripheral and neuroanatomical alterations. Our work will lead to improved methods of earlier diagnosis of Parkinson's, identify new molecular targets for therapy, and generate new improved models for testing neuroprotective treatments.

Lay Summary
Further information available at:

Types:
Investments > €500k

Member States:
United Kingdom

Diseases:
Parkinson's disease & PD-related disorders

Years:
2016

Database Categories:
N/A

Database Tags:
N/A