Glucocerebrosidase mutations in Parkinson disease:molecular pathogenesis,and the basis for personalised therapy with small molecule chaperones

https://neurodegenerationresearch.eu/survey/glucocerebrosidase-mutations-in-parkinson-diseasemolecular-pathogenesisand-the-basis-for-personalised-therapy-with-small-molecule-chaperones/

Principal Investigators

Professor AH Schapira

Institution

University College London

Contact information of lead PI
Country

United Kingdom

Title of project or programme

Glucocerebrosidase mutations in Parkinson disease:molecular pathogenesis,and the basis for personalised therapy with small molecule chaperones

Source of funding information

MRC

Total sum awarded (Euro)

€ 1,293,921

Start date of award

01/02/2015

Total duration of award in years

4.0

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords
Research Abstract

This application addresses the challenge of slowing the clinical and pathological progression of Parkinson disease (PD) with the use of small molecule chaperones to enhance the activity of glucocerebrosidase enzyme (GCase) activity in turn to reduce alpha-synuclein levels and retard neurodegeneration. The programme will use a large cohort of >200 individuals with GBA mutations already recruited from the National Lysosomal Storage Disorders services at the Royal Free London and Addenbrokes hospitals. We propose to phenotype our expanded cohort for these parameters and to retest our complete group to identify progression of the abnormalities or conversion to clinically diagnostic PD. The objectives of this Pathfinder grant are to: 1. Define the clinical evolution and phenotype of GBA mutation positive individuals as they progress to the development of PD. This will enable these features to be correlated with the underlying biochemical abnormalities. 2. Investigate the mechanisms of glucocerebrosidase enzyme (GCase) deficiency in patient derived primary (fibroblast) cultures obtained from our established cohort of GBA mutation positive individuals, age-matched non-GBA mutant PD patients and controls. 3. Determining the effect of small molecule chaperones to enhance GCase activity and reduce alpha-synuclein levels in patient cells and in animal models of human mutations to establish the validity of pursuing these as the next step as a therapy to slow progression in PD patients.

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