Investigation of the pathogenic basis of the tau gene association with neurodegeneration

https://neurodegenerationresearch.eu/survey/title-of-piinvestigation-of-the-pathogenic-basis-of-the-tau-gene-association-with-neurodegeneration/

Title of project or programme

Title of PI Investigation of the pathogenic basis of the tau gene association with neurodegeneration

Principal Investigators of project/programme grant

Title	Forname	Surname	Institution	Country
Dr	Rohan	de Silva	University College London	UK

Address of institution of lead PI

Institution	University College London
Street Address	UCL Institute of Neurology, 1 Wakefield Street
City	London
Postcode	WC1N 1PJ

Country

- United Kingdom

Source of funding information

Medical Research Council

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1004272.84

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Total duration of award in months

60

The project/programme is most relevant to

- Neurodegenerative disease in general

Keywords

Research abstract in English

Tauopathies are the class of neurodegenerative disorders characterised by pathological inclusions containing fibrillar deposits of the microtubule-associated protein, tau. The tau gene (MAPT) is mutated in frontotemporal dementia with parkinsonism with tau pathology linked to chromosome 17 (FTDP-17T) and, though not mutated, the H1 haplotype of MAPT is highly associated with

progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD) and, to a lesser extent, with sporadic Parkinson?s disease (PD). We have succeeded in describing the full extent of the MAPT haplotype to a region of near complete linkage disequilibrium (LD) extending over about 1.8 million base pairs and have identified sub-haplotypes within this region, particularly in MAPT itself and MAPT promoter polymorphisms affecting the core promoter and putative conserved enhancer domains that are more associated with PSP, CBD and Alzheiimer s disease (AD). Furthermore, recent findings show that the extended LD of the MAPT region is caused by a large genomic inversion and this region is subject to further chromosomal rearrangements including deletions and multiplications. In this work, we propose a systematic approach to study the potential effects of the MAPT gene polymorphisms and the gross genomic rearrangements on the expression and splicing of MAPT and genes in flanking regions. We will map the inverted chromosomal region in order to identify any disease-specific, pathogenic configurations, including partial and complete deletion or multiplication of genes.

Lay summary
In which category does this research fall?

- Basic research