Molecular basis of frontotemporal dementia and related disorders

https://www.neurodegenerationresearch.eu/survey/molecular-basis-of-frontotemporal-dementia-and-related-disorders/

Title of project or programme

Molecular basis of frontotemporal dementia and related disorders

Principal Investigators of project/programme grant

Title	Forname	Surname	Institution	Country
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- United Kingdom

Source of funding information

Medical Research Council

Total sum awarded (Euro)

1307948.19

Start date of award

01-04-2005

Total duration of award in months

60

The project/programme is most relevant to

- Alzheimer’s disease and other dementias
- Neurodegenerative disease in general

Keywords

Research abstract in English

Frontotemporal dementia (FTD) is the second most common form of presenile dementia after Alzheimer's disease, making it of major clinical significance. We recently showed that a mutation in the CHMP2B gene was responsible for causing FTD in a large Danish family. The CHMP2B mutation leads to the formation of aberrant CHMP2B proteins that affect endosomal function. There is accumulating evidence that endosomal dysfunction may underlie a number of neurodegenerative diseases including Alzheimer's disease and motor neurone disease.

The aim of this programme is to further understand the role of CHMP2B and related genes in the pathogenesis of FTD and other neurodegenerative diseases. This research may give insight into the aetiology of a number of neurodegenerative disorders.

The specific research objectives are:

1) To develop mouse models of CHMP2B induced neurodegeneration. This will allow further characterisation of the pathogenic cascade that leads to disease and the eventual testing of therapeutics. We will use transgenic mice over-expressing CHMP2B mutant proteins as well as CHMP2B knockout mice. Development of these mouse lines will also allow crossing to other mouse models of neurological diseases in order to identify common pathways of neurodegeneration.

2) To further characterise CHMP2B and related genes in human tissue. This aim includes genetic analysis to understand the wider impact of CHMP2B and related genes in neurological diseases. We are also analysing brain tissue from patients with a range of neurological diseases to identify CHMP2B induced pathologies as well as endosomal pathology.

3) To develop cell culture models of CHMP2B related cell death This aim will allow us to study the mechanisms and cell death pathways that lead to neurodegeneration in well characterised cell lines and in primary neuronal cultures. The use of cell culture allows a number of different cell death paradigms to be investigated, as well interactions with other neurological disease genes.

In summary, the research aims of this programme may give insight into the pathogenesis of FTD as well as other neurodegenerative disorders.

Lay Summary