Transgenic modelling of human prion diseases, intermammalian transmission barriers & assessing candidate therapeutics

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Title of project or programme

Transgenic modelling of human prion diseases, intermammalian transmission barriers & assessing candidate therapeutics

Principal Investigators of project/programme grant

Title	Forname	Surname	Institution	Country
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Address of institution of lead PI

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- United Kingdom

Source of funding information

Medical Research Council

Total sum awarded (Euro)

7586728.95

Start date of award

01-04-2005

Total duration of award in months

60

The project/programme is most relevant to

Prion disease

Keywords

Research abstract in English

“In studies now spanning well over a decade we have developed highly specialised transgenic transmission facilities for comprehensive studies of human prion disease under appropriate biocontainment. Species-barrier-free transmission of many forms of human prion disease is available. While excellent, well characterised models are now in routine use, further improvement to these models, and the development of improved models for the assay of vCJD prions are underway. In addition to ongoing basic research into intermammalian and strain-specific transmission barriers and characterisation of the prion strains causing human disease, this facility is being applied to address key public health issues which require human prion bioassay (tissue distribution of infectivity and human prion decontamination for example) and to study putative prion therapeutics. Animal models of a range of inherited human prion diseases are being studied, in particular to determine if prions are produced spontaneously in such animals.

The specific aims of this programme are as follows:

1) Provision of Transgenic Core Facility for the Unit

2) Transgenic modelling of human susceptibility to BSE and vCJD: Effect of codon 129 polymorphism.

3) Production and characterization of transgenic models for bioassay of putative synthetic prions.

4) Use of speed congenics to reduce genetic background effects

5) Transgenic modelling of inherited human prion diseases.

6) Production of human PrP glycosylation-deficient models for studying the role of PrP glycosylation in prion strain variation

7) Generation of human prion susceptible cell lines from human PrP/SV40 T-antigen double transgenic mice.

8) Evaluation of potential therapeutic agents”

Lay Summary