Human molecular genetics and bioinformatics

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Title of project or programme

Human molecular genetics and bioinformatics

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)

5521862.50

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

“The MRC Prion Unit Human Molecular Genetics of Prion and Related Dementias Programme investigates why some people, but not others, get prion diseases such as Creutzfeldt-Jakob disease (CJD). By comparing genetic differences between people who developed CJD and healthy people we hope to identify genes that influence why particular people are more susceptible to these diseases,

and use this information to better estimate public health risks and to develop new tests and treatments. We also know that the fundamental processes involved in CJD, where one of the body's own proteins becomes misshapen and then forms large clumps of material, are very relevant to other much commoner diseases such as Alzheimer's Disease. Evidence in support of the involvement of non- PRNP genetic factors comes in part from work with laboratory inbred mouse strains, detailed in this group's section. A small number (~5) of quantitative trait loci (QTL) responsible for determining incubation time following intra-cerebral inoculation with prions have been mapped by the MRC Prion Unit and others using different crossing strategies and prion strains. The integration of unbiased genome-wide strategies in mouse and human prion disease will be an important in the success of both programs. Our discovery research utilises recently available genome-wide genotyping technologies. We have successfully conducted a pilot genome-wide association study with EA-Affymetrix 500K arrays (Mead et al. Lancet Neurology 2009). The necessary molecular genetic, bioinformatic, and statistical genetic expertise for genome-wide association study is either available in the Unit or through collaboration. Over the next few years we expect to develop our discovery genome-wide association research in larger patient cohorts using more advanced genotyping technologies, and focus on developing cellular and animal models to test the genes identified in our discovery research. It has become increasingly apparent that neurodegenerative diseases share fundamental mechanisms involving protein misfolding, including Alzheimer's disease and Parkinson's disease. It is likely that genetic modifiers of prion pathogenesis may be of broader relevance to other protein misfolding diseases, and we intend to explore these possibilities. One of the key goals of bioinfomatics in the Unit is to identity modifier genes, pathways and mechanisms controlling prion pathogenesis. The objective of this aspect of the programme is to use computational and statistical methods for the analysis and integration of these Unit based large-scale experiments (and also externally generated data sets) and their resulting data sets, which are large, inherently noisy and do not produce necessarily clear candidates."

Lay Summary