Human molecular genetics and bioinformatics

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Principal Investigators

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Country

United Kingdom

Title of project or programme

Human molecular genetics and bioinformatics

Source of funding information

MRC

Total sum awarded (Euro)

€ 9,153,942

Start date of award

01/04/2011

Total duration of award in years

5.0

The project/programme is most relevant to:

Prion disease

Keywords
Research Abstract

Prion diseases in both humans and animals are characterised by a long, silent incubation periods before the disease emerges and this time interval varies greatly between individuals. Differences in our genetic makeup are a key factor in this variability. We already know that natural variation within one key gene, the prion protein gene, has a major influence on incubation time but it is now clear that a number of other genes are also important. If we can identify these genes and then find out what they do and how they vary between individuals we will have a much better understanding of the disease and why some individuals exposed to BSE

have developed variant CJD and others have not. It may be that many others are infected but are still incubating the disease and the identification of these genes should allow much better predictions of any human epidemic. Such information should also cast light on the fundamental processes involved in these diseases and may provide new targets for drug therapies.||Identifying such genes in humans is extremely challenging and we have chosen to start our search in laboratory mice. Genetic studies of large mouse families have enabled us to narrow our search from the many thousands of genes down to a few hundred. We then look in detail at the DNA sequence of these candidate genes to find the small number of genes of importance. To show we have found the correct genes we will evaluate them in a cell based system to see if the gene influences cell susceptibility and prion replication. The ultimate proof that we have the right gene is provided by modifying the gene in mice and seeing if that actually results in the expected change in incubation period. Mice have largely the same genes as humans and so if we can find the key genes in mice, we can readily find their human counterparts. To test whether a candidate gene identified in our mouse studies is also important in human prion diseases we will search for variation in the equivalent human gene and use statistical analysis to test whether there is a link between genetic difference and susceptibility to human prion diseases such as variant CJD. Prion diseases share many features with other diseases of the ageing brain therefore the genes identified in these studies are expected to identify pathways and new therapeutic targets that are of wider relevance in neurodegeneration.

Lay Summary
Further information available at:

Types:
Investments > €500k

Member States:
United Kingdom

Diseases:
Prion disease

Years:
2016

Database Categories:
N/A

Database Tags:
N/A