PERADES

Defining Genetic, Polygenic and Environmental Risk for Alzheimer's Disease using multiple powerful cohorts, focussed Epigenetics and Stem cell metabolomics

The PERADES collaboration aimed to identify new genes influencing the risk of developing Alzheimer's disease (AD). We used powerful case-control study designs to identify 6 novel genome-wide significant genetic associations, disseminated in several high-profile publications.

We have further refined the use of these genetic results in predicting an individual's risk of developing Alzheimer's disease. Indeed, we are now able to correctly predict disease status around 80% of the time and can identify people with high or low AD risk with over 90% accuracy. Our work has increased the evidence that immunity is playing a significant contribution to AD and also implicates lipid processing, endocytosis, ubiquitination and A β processing, as pathways involved in disease development.

Combining data from genetics, gene expression and protein-protein interaction experiments has allowed us to identify gene networks that harbour genetic variation significantly enriched in individuals with AD. Subsequent work utilising the PERADES data has been being central to identifying further genetic risk loci, including rare variant associations in the coding regions of genes, which can be more easily modelled in cells, flies or other model systems, to more quickly identify disease mechanisms and therapies.

We are now modelling combinations of genetic risk and developing induced pluripotent stem cell models from individuals with the highest and lowest genetic risk profiles for disease. This work will be used within the UK Dementia Research Institute at Cardiff to understand disease mechanisms and test new drugs to help protect or treat AD in the future.