Prevention and early diagnosis for Alzheimer's disease: Gene expression profiling study in a case-control elderly population in Illawarra region

Summary of final report

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Overview

The majority of Alzheimer's disease research has focused on the brain. However this innovative project, supported by IRT Foundation, involves a search for genetic markers for Alzheimer's disease in saliva samples. The researchers are comparing gene expression, and microRNA levels in target genes between participants with and without Alzheimer's disease. Ultimately, the goal of this project is to develop a blood or saliva test for the detection of the early onset of the disease.

Aims and objectives

Alzheimer's disease (AD), the most common form of age-related dementia, affects around 6.5% of persons in Australia aged over 65 years. AD is a progressive, neurodegenerative disease characterized clinically by a gradual cognitive decline including loss of memory, orientation and reasoning. Currently there is no simple definitive test to diagnose AD. Hence there is considerable interest in a reliable early detection system. Despite recent progress in genetic research, gene testing is currently not sufficiently reliable for most individuals and has limited utility for predictive purposes. This project hopes to increase the value of genetic testing for both patients and their relatives. We have drawn a parallel between the phenotypic (i.e. observable) information reported for each participant with the gene expression with the aim of getting a better understanding of the pathophysiology of this disorder. This result will allow us, as a preventative approach, to act prior the development of the disease. Furthermore, this work may lead to the establishment of a specific diagnostic test and in the future, to the development of effective therapy for this devastating disease.

Main results

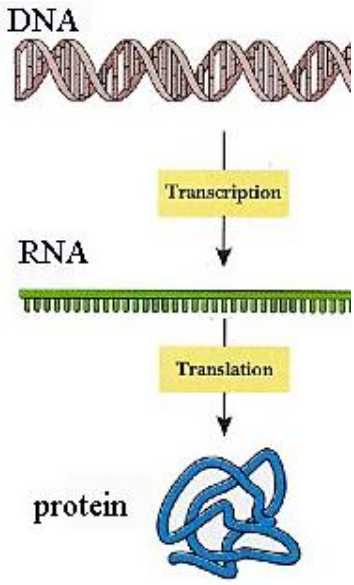
This is the first study exploring both genetic and phenotypic (i.e. observable) aspects of Alzheimer's disease (AD) using saliva samples. We have established for each participant a complete neuropsychiatric and clinical profile including lifestyle information. We have studied the difference in gene expression in AD sufferers and their matched controls for age and gender according their reported phenotypic information. We have developed a bank of DNA (genetic material specific for each individual) and neuropsychiatric and clinical profiles (incorporating lifestyle information) for AD patients. This is the first genetic population established for Alzheimer's disease in the greater Illawarra and South Sydney area. This is a valuable asset for both the current and future projects.

By utilising a new technology known as a "transcriptome gene expression array", we have identified differences in the expression of genes in the population involved in the genetic susceptibility for AD in small fragments of the genome. Until now, these had previously not been characterized (microRNA). We have characterized different genetic profiles between Alzheimer's disease sufferers and their matched controls, confirming our hypothesis. We are currently in the process of double-checking this finding using another method more sensitive (although a lot more time consuming)

than the transcriptome array already performed (Real Time- PCR), focusing on the genes of interest, before the publication of this innovative work in a high impact factor journal.

Moreover, the most novel aspect of this project was the establishment of a complete genetic profile, using saliva samples (with the majority of current genetic AD research utilizing post-mortem brain tissues) with the aim of developing a proper genetic diagnostic profiling.

In addition to exploring the genetic difference between AD patients and their matched controls, we have added a younger control group to examine the effects of ageing on the tested genotypic and phenotypic tested parameters. This type of genetic analysis has never been explored in the context of ageing studies. By adding this "young" control group, we can clearly determine the genetic changes which are specific to AD (differential genetic profiles between AD versus their matched "old" controls) or due to normal ageing ("young" controls versus "old" controls).



DNA = Genes (including "silent" and coding sections)

RNA = Contains only coding sections for amino-acids

Protein = Sequence of amino-acids coded by RNA

This project was funded through a grant from IRT Foundation. IRT Foundation (formerly IRT Research Foundation) directly aligns with IRT Group's mission to create age-friendly communities where older Australians can age without barriers.

Since 2009, the Foundation has supported research projects promoting a greater understanding of the ageing process and the care and wellbeing of seniors. Over $1.6M in grants have been awarded to leading Australian researchers. IRT Foundation also funds community grants and educational activities.

By making a commitment to research, advocacy programs and partnering with the community, IRT Foundation funds programs and services which help create age-friendly communities and change people's perceptions of older Australians and ageing. IRT Foundation is a key pillar of IRT Groups commitment to enrich 20,000 lives and give back $20 million in community dividends by 2020.

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