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Inflammatory gene expression profiles in sporadic, familial and *TREM2* variant Alzheimer's disease

Introduction: The underlying pathogenesis of Alzheimer's disease (AD) remains elusive. However recent genetic observations indicate that neuroinflammation may play a role in the causative mechanism. Links have been identified between some inflammatory genes identified in GWAS studies and other genes specifically associated with AD such as *APOE* and *TREM2*, providing further reasoning to investigate the role of neuroinflammation in AD. Here we explore the gene expression profiles of 256 inflammatory genes in post-mortem AD brains of sporadic and familial origin.

Material and methods: The frontal cortex from post-mortem brain samples were collected from sporadic AD cases (n=10), familial AD cases (n=7), *TREM2* variant cases (n=7) and neurologically normal controls (n=6). RNA was extracted and quality checked using the Qiagen RNeasy kit and Eppendorf spectrophotometer. The samples were analysed using the human inflammation panel (NanoString Technologies) and an additional 30 genes already identified to be implicated in AD.

Results: 286 genes were successfully processed and analysed using NanoString Technologies nSolver software. All pairwise comparisons were made and T-tests completed with a number of significant gene expression changes. When compared to controls, 126 genes had statistically different expression levels ($p < 0.05$) in sporadic AD cases, 93 genes in familial AD cases and 57 genes in the *TREM2* variant cases. The expression profile of the *TREM2* variant group overlapped with the sporadic AD cases. Pathway analysis were performed using WebGestalt to look at GO (gene ontology) and KEGG (Kyoto Encyclopedia of Genes and Genomes) analyses.

Conclusions: As predicted there is a strong inflammatory component to AD with differing expression of inflammatory markers. This suggests that neuroinflammation plays a large role in AD pathogenesis. Inflammatory gene expression also differs between sporadic AD cases and familial AD cases indicating that the two disease groups may not share a common inflammatory response pathway. Further investigations into the individual gene targets and their mechanisms of action in AD pathogenesis are needed to identify their influence on the underlying disease mechanisms.