Abstract Topic: A1.j. β-Amyloid Diseases, Disease Mechanisms, Pathophysiology: Astroglia

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INVESTIGATING THE ROLE OF ASTROCYTES IN *TREM2* VARIANT CASES

Objectives: *TREM2,* a genetic risk factor for late onset Alzheimer's disease (AD), is involved in inflammation. However, the full role of TREM2 in AD is unclear. Astrocytes form barriers around amyloid plaques to protect neurons from inflammation and are involved in Aβ clearance through mediators such as APOE. TREM2 and APOE have been identified to act along similar pathways. TREM2 and astrocytic mechanisms could be linked through APOE. We investigate the genetic, proteomic and pathological astrocytic profile in human *TREM2* variant cases compared to sporadic AD (SAD), familial AD (FAD) or control human post-mortem brains.

Methods: Frontal cortex was collected from SAD (n=10), FAD (n=7), *TREM2* variant AD cases (n=3), *TREM2* variant controls (n=2) and control cases (n=6). RNA samples were analysed using the Nanostring inflammation panel. Proteins were extracted before mass spectrometry was performed. Immunohistochemistry for each case was performed using GFAP, an astrocytic marker, and analysed to determine the astrocytic load.

Results: Genetic and proteomic results highlighted that GFAP gene and protein expression increases across all AD groups with *TREM2* variant AD cases showing the most marked increase compared to controls (2.35-fold nanostring, 3.76-fold proteomics). Pathological analysis indicates that *TREM2* variant AD cases have no statistical difference in GFAP load than SAD and FAD cases.

Conclusions: *TREM2* variant AD cases have a different astrocytic profile when compared to other AD cases. Further investigation into the role astrocytes play in AD and how TREM2 interacts with these pathways may give insight into the risk that *TREM2* variant cases bring.