Dissecting ABCA7's role in Alzheimer's Disease Through Microglial Transcriptomics

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The ATP-binding cassette subfamily A member 7 (ABCA7) gene, initially identified as a major risk factor for Alzheimer's disease (AD) through genome-wide association studies (GWAS), exhibits a distinct expression pattern in the brain with the highest expression levels found in microglia. Previous studies indicated ABCA7's involvement in microglial phagocytosis. We aimed to examine how changes in ABCA7 expression in microglia impact gene expression between phenotypes and between microglial subtypes across phenotypes. We performed single-nuclei RNA sequencing (10X genomics) on the BA10 region of nine ABCA7 mutation carriers, six AD non-carriers and eight cognitively healthy controls. After integration with RPCA, harmony and ambient RNA removal with DecontX, microglia were isolated. We performed subtyping of the microglia with the FindMarkers function from Seurat. We could identify homeostatic, ribosomal response, disease associated, cytokine response, antigen presenting response and neuronal marker microglia. We see differences in cell type proportions between the three different phenotypes. Preliminary analysis revealed promising differentially expressed genes. Eventually we will link these changes in gene expression to pathways that could link ABCA7 to AD risk and further decipher the role of microglia in AD.