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A single-cell atlas of cerebrospinal fluid in Alzheimer's disease

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Abstract

Background: Potential differences in immune characteristics between sporadic late-onset Alzheimer's disease (sLOAD) and sporadic late-onset AD (sEOAD) have not been well elucidate. Immune cells in the cerebrospinal fluid (CSF) can reflect the brain immune system dysregulation of patients.

Method: Here, we collected CSF of 9 sEOAD patients, 6 sLOAD patients, 11 age-matched controls for sEOAD, and 10 age-matched controls for sLOAD from patients in the China Aging and Neurodegenerative Initiative (CANDI) cohort, and performed single-cell RNA sequencing (scRNA-seq) and single-cell TCR sequencing (scTCR-seq), obtaining a total of 52,719 single cells for further bioinformatics analysis.

Result: We found a reduction in the proportion of T cells and an increase in the proportion of microglia-like macrophages in the samples of AD patients. Microglia-like macrophages upregulate inflammation genes in AD patients. The proportion of clonally expanded CSF T cells in sLOAD patients was higher, indicating that antigen-specific T cells play a greater role in the disease process of sLOAD.

Conclusion: We revealed differences in the transcriptional signatures of immune cells in the CSF of sLOAD and sEOAD. In further studies, we plan to collect the publicly available scRNA-seq of brain from AD patients with age of disease onset information and combine these with our scRNA-seq data of CSF for integrated analysis to reveal the potential interactions between immune cells in CSF and brain parenchyma.