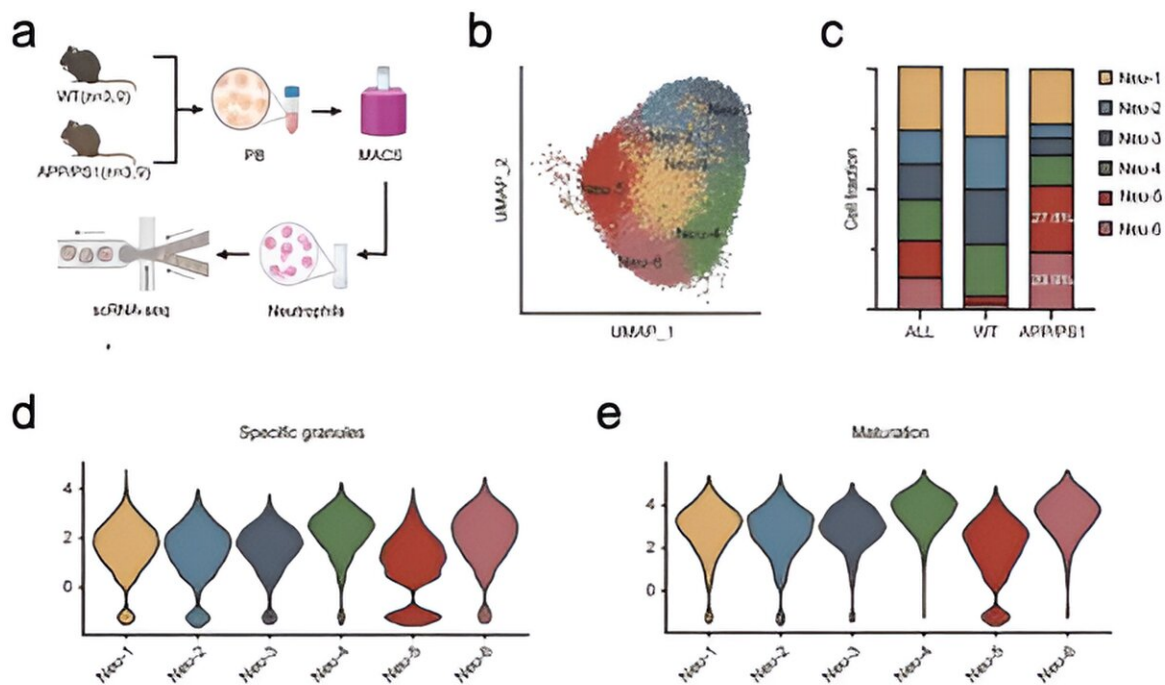


Unique neutrophil type associated with Alzheimer's disease identified

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Single-cell RNA sequencing of peripheral blood neutrophils from APP/PS1 mice. (Image by LV et al.). Credit: usth

Researchers have identified a unique type of neutrophil significantly associated with Alzheimer's disease (AD) pathology and mapped the transcriptome of neutrophils in the peripheral blood of AD mice. The study was [published](#) in *Immunity & Ageing*. The team includes Lv

Xinyou from the University of Science and Technology of China (USTC), in collaboration with Associate Researcher Li Jin from the School of Public Health.

AD, a leading cause of dementia among the elderly, is characterized by the accumulation of amyloid-beta plaques and tau tangles in the brain, resulting in neuronal loss and cognitive decline. While extensive research has been conducted, the mechanisms involving immune cells in AD progression remain inadequately understood.

The study, therefore, aimed to explore the heterogeneity of neutrophils, a type of white blood cell, in the context of AD. Researchers isolated neutrophils from the peripheral blood of AD model mice, specifically 7-month-old female APP/PS1 [transgenic mice](#) and 5xFAD transgenic mice, both well-established models for studying AD.

These neutrophils were then subjected to scRNA-seq, a method that allows for the analysis of gene expression at the individual cell level, providing a comprehensive view of cellular diversity.

The data generated from scRNA-seq were processed using the 10x Genomics Cell Ranger software, with stringent quality control measures applied to ensure accuracy. This included filtering out cells with extreme gene counts, high unique molecular identifiers (UMIs), and elevated mitochondrial gene content.

The analysis revealed six distinct neutrophil clusters. Among these, the Neu-5 cluster was notably enriched in AD mice. This cluster displayed unique characteristics, including fewer specific granules and a lower maturity score compared to other neutrophil types, suggesting a specialized role in AD pathology.

Further gene ontology analysis indicated that the Neu-5 cluster had

downregulated genes involved in cytokine-mediated signaling pathways, pointing to an altered inflammatory response.

A particularly noteworthy finding was the upregulation of the *Ccrl2* gene within this [cluster](#). This upregulation was validated through [flow cytometry](#) and immunohistochemical staining, which confirmed the increased expression of the CCRL2 protein in the brains of AD mice.

The study is crucial for understanding how these [immune cells](#) contribute to AD progression and opens the door to potential new therapeutic targets focused on modulating immune responses.

More information: Xiaolin Zhang et al, Single cell transcriptome analysis identified a unique neutrophil type associated with Alzheimer's disease, *Immunity & Ageing* (2024). [DOI: 10.1186/s12979-024-00448-x](https://doi.org/10.1186/s12979-024-00448-x)

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