Medical Xpress

Single-cell RNA-seq reveals transcriptomic modulation of Alzheimer's disease by activated protein C

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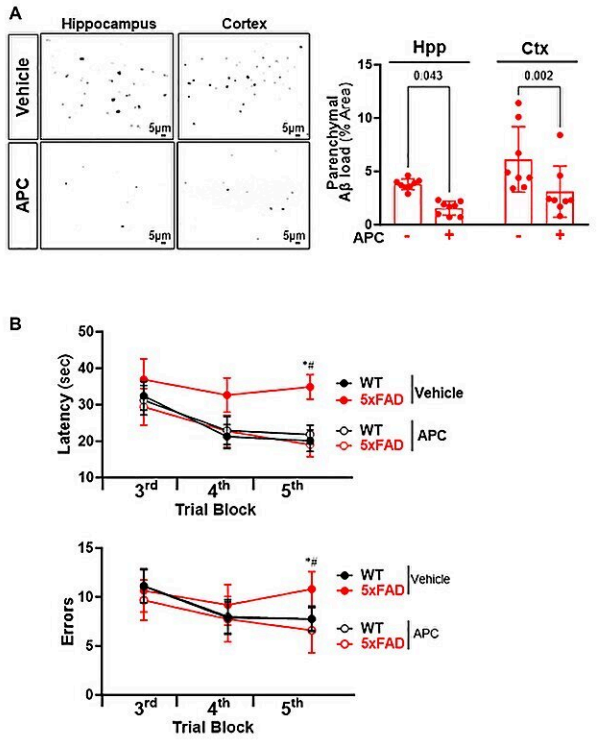

(A) Representative images and quantification of Aβ stained with thioflavin S in the hippocampus and cortex of 5xFAD mice treated with or without APC. (B) Radial arm water maze test showed the latencies to hidden platform and the errors happens in arms in WT and 5xFAD mice. $N = 8$, $^{*}p$ $^{\#}p$ Aging (2024). DOI:

10.18632/aging.205624

A new research paper titled "Single-Cell RNA-seq reveals transcriptomic modulation of Alzheimer's disease by activated protein C" has been published in *Aging*.

In this new study, researchers Mohammad Kasim Fatmi, Hao Wang, Lily Slotabec, Changhong Wen, Blaise Seale, Bi Zhao, and Ji Li from the University of South Florida, University of Mississippi Medical Center and the G.V. (Sonny) Montgomery VA Medical Center used single-cell RNA sequencing and bioinformatic analysis to analyze the effects of APC [Activated Protein C] treatment on AD transgenic mice.

"In our investigation, we utilized transgenic mice that contain expression for five major amyloid pathologies that allow for rapid progression of AD and Aβ deposition known as 5xFAD mice," the team writes.

The returned sequencing data was processed through the 10x Genomics CellRanger platform to perform alignment and form corresponding matrix to perform bioinformatic analysis. Alterations in glial cells occurred in 5xFAD versus WT, especially increases in microglia proliferation were profound in 5xFAD. Differential expression testing of glial cells in 5xFAD versus WT revealed gene regulation. Globally, the critical genes implicated in AD progression are upregulated such as Apoe, Ctsb, Trem2, and Tyrobp.

Using this differential expression data, GO term enrichment was completed to observe possible biological processes impacted by AD progression. Utilizing anti-inflammatory and cyto-protective

recombinant Activated Protein C (APC), the researchers uncovered inflammatory processes to be downregulated by APC treatment in addition to recuperation of nervous system processes. Moreover, animal studies demonstrated that administration of recombinant APC significantly attenuated Aβ burden and improved cognitive function of 5xFAD mice.

"The downregulation of highly expressed AD biomarkers in 5xFAD could provide insight into the mechanisms by which APC administration benefits AD," the researchers conclude.

More information: Mohammad Kasim Fatmi et al, Single-Cell RNA-seq reveals transcriptomic modulation of Alzheimer's disease by activated protein C, *Aging* (2024). DOI: 10.18632/aging.205624

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