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Exploring the Associations between Alzheimer's Disease and GBM Mediated by Microglia Based on Network Analysis

C Zhang [1], X Zhong, L Yi, Z Zhao, Y Zhang, G Tan, Y Zhang, Y Zhang, Y Xu, N Wu

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Abstract

Previous studies have revealed that there existed epidemic associations between Alzheimer's disease (AD) and many types of tumors, however, the inner biological mechanism connecting these diseases was not clear currently. In this study, we explored the transcriptome associations between AD and glioblastoma multiforme (GBM) that both originate in the brain, using microglia as a bridge, from gene and network levels. Firstly, we extracted human scRNA sequencing datasets from Gene Expression Omnibus (GEO) database, and identified differentially expressed genes within microglia after cell annotation. It was observed that there were 11 common genes shared by AD and GBM dys-regulated genes. Next, we utilized DIAMOnD and Flow Centrality algorithms to identify microglia modules and mediating pathways connecting these two diseases based on global network topology. Among these candidate pathways, the mediating genes FURIN and BACE1 (from SPIKN5 to CSNK1A1) were not only related to the formation of amyloid beta plaques that accumulate in the brain of AD patients, but also involved in cancer biology. Furthermore, the biological explorations of mediating pathways connecting AD and GBM modules reveal inflammatory response, lipid metabolism disorder, and cell proliferation terms. Finally, novel signatures for early AD detection as well as risk models for glioma prognosis were identified based on mediating genes involved in these pathways. In conclusion, this study provided a novel network-based strategy for exploring microglia mediation between AD and GBM and identified candidate signatures for disease detection and prognosis.

Keywords: Alzheimer’s disease; glioblastoma multiforme; microglia; network analysis; scRNA-seq.