Comparative Transcriptomic Analysis of Alzheimer's Disease Across Diverse Populations for Target and Pathway discovery

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Abstract

Alzheimer's disease (AD) is a complex disorder with numerous known risk factors which may vary across populations, yet the underlying molecular mechanisms of these variations are rarely addressed. This study aims to perform comparative transcriptomic analysis of different populations to analyse these regulatory patterns linked to Alzheimer's disease. Bulk RNA-Seq datasets from hippocampal tissue of 4 Populations (Chinese, Japanese, American, Italian) were obtained from NCBI GEO. Using these, differentially expressed genes (DEGs) were identified. The functional enrichment of DEGs (Gene Ontology (GO) and Reactome pathway analysis) were performed using enrichR. The protein-protein interaction (PPI) network were constructed using STRING database and Cytoscape in order to identify the hub genes of each population. A competing endogenous RNA (ceRNA) network was built based on predicted miRNA–lncRNA–mRNA interactions. The drug-gene interactions were analysed using the Drug-Gene Interaction Database (DGIdb) with the hub genes as input. The DEG profiles and the pathway enrichment were seen to be distinct in different populations, highlighting the molecular heterogeneity of AD. The GO and Reactome analysis revealed that synaptic dysfunction and neuroinflammatory pathways were common among all populations. However, pathways like epigenetic regulation, vitamin metabolism and immune response modulation were seen to be population specific. The top hub genes were also distinct across populations. The ceRNA network revealed that lncRNAs like NEAT1, XIST, MALAT1 which have significant role in neurodegeneration ,were commonly associated with multiple Hub gene-miRNA interactions. This reflects their potential as key regulatory lncRNAs. This comparative study reveals population specific variations in the pathology of AD. Understanding these differences is important to determine whether the current treatment methods are universally applicable or more population specific approaches are needed. The identified hub genes and their regulatory networks act as promising targets for developing precision, population-specific interventions in AD research.

Keywords: Alzheimer's Disease, Cognitive Decline, RNA-Seq