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Identification of Blood Biomarkers Unveiling Early Alzheimer's Disease Diagnosis Through Single-Cell RNA Sequencing Data and Autoencoders

Authors : Hediyeh Talebi, Shokoofeh Ghiam, Changiz Eslahchi

Abstract : Traditionally, Alzheimer’s disease research has focused on genes with significant fold changes, potentially neglecting subtle but biologically important alterations. Our study introduces an integrative approach that highlights genes crucial to underlying biological processes, regardless of their fold change magnitude. Alzheimer's Single-cell RNA-seq data related to the peripheral blood mononuclear cells (PBMC) was extracted from the Gene Expression Omnibus (GEO). After quality control, normalization, scaling, batch effect correction, and clustering, differentially expressed genes (DEGs) were identified with adjusted p-values less than 0.05. These DEGs were categorized based on cell-type, resulting in four datasets, each corresponding to a distinct cell type. To distinguish between cells from healthy individuals and those with Alzheimer's, an adversarial autoencoder with a classifier was employed. This allowed for the separation of healthy and diseased samples. To identify the most influential genes in this classification, the weight matrices in the network, which includes the encoder and classifier components, were multiplied, and focused on the top 20 genes. The analysis revealed that while some of these genes exhibit a high fold change, others do not. These genes, which may be overlooked by previous methods due to their low fold change, were shown to be significant in our study. The findings highlight the critical role of genes with subtle alterations in diagnosing Alzheimer's disease, a facet frequently overlooked by conventional methods. These genes demonstrate remarkable discriminatory power, underscoring the need to integrate biological relevance with statistical measures in gene prioritization. This integrative approach enhances our understanding of the molecular mechanisms in Alzheimer’s disease and provides a promising direction for identifying potential therapeutic targets.

Keywords : alzheimer's disease, single-cell RNA-seq, neural networks, blood biomarkers
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