Identification of immune cell infiltration and biomarkers in Alzheimer's disease and COVID-19 by integrated bioinformatics analysis and machine learning

Juntu Li
The Affiliated Suzhou Hospital of Nanjing Medical University

Linfeng Tao
The Affiliated Suzhou Hospital of Nanjing Medical University

Yanyou Zhou
The Affiliated Suzhou Hospital of Nanjing Medical University

Yue Zhu
The Affiliated Suzhou Hospital of Nanjing Medical University

Chao Li
Suzhou Municipal Hospital

Yiyuan Pan
Suzhou Municipal Hospital

Jun Liu
liujunphd@sina.cn
The Affiliated Suzhou Hospital of Nanjing Medical University

Research Article

Keywords:

Posted Date: April 11th, 2024

DOI: https://doi.org/10.21203/rs.3.rs-4221649/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

Additional Declarations: No competing interests reported.
Abstract

Background: Since its emergence in late 2019, COVID-19 has become a global epidemic, resulting in numerous infections, including a significant number of critically ill patients. Several studies have suggested a possible link between Alzheimer’s disease (AD) and COVID-19. For instance, a Mendelian randomization study has proposed a causal relationship between Alzheimer’s disease and COVID-19 in the pathogenic mechanism. However, there are limited studies exploring the common pathogenic genes and immune infiltration between the two. Therefore, we conducted this study to identify key genes in COVID-19 associated with Alzheimer’s disease, evaluate their correlation with immune cell characteristics and metabolic pathways, and investigate potential novel biomarkers.

Methods: Transcriptome analyses were used to identify common biomolecular markers of AD and COVID-19. Differential expression analysis and weighted gene co-expression network analysis (WGCNA) were performed on gene chip datasets (GSE213313, GSE5281, and GSE63060) from AD and COVID-19 patients to identify genes associated with both conditions. Common pathogenic molecular mechanisms were identified through Gene Ontology (GO) enrichment analyses. The core genes were then identified using machine learning methods. Subsequently, we evaluated the relationship between these core genes and common immune cells and metabolic pathways. Finally, our findings were validated through single-cell analysis.

Results: The study identified 484 common differentially expressed genes (DEGs) by taking the intersection of genes between AD and COVID-19. The black module, containing 132 genes, showed the highest association between the two diseases according to WGCNA. GO enrichment analysis revealed that these genes mainly affect inflammation, cytokines, immune-related functions, and signaling pathways related to metal ions and cellular response to viruses. Additionally, a machine learning approach identified eight core genes. We identified links between these genes and immune cells and also found a strong association between EIF3H and oxidative phosphorylation. In addition, these results were further validated by single-cell analysis.

Conclusion: This study identifies potential shared genes, signaling pathways, immune-related alterations, and changes in metabolic pathways that may collectively contribute to the pathogenesis of COVID-19 and Alzheimer’s disease. These findings provide new targets for the diagnosis and treatment of both diseases.

Introduction

COVID-19, caused by the SARS-CoV-2 virus, primarily spreads through droplet and airborne transmission, resulting in respiratory symptoms and complications. This highly contagious virus has led to over 6.9 million deaths worldwide. In some patients, infection triggers a cytokine storm, prompting an excessive immune response, systemic inflammation, and tissue damage. Due to its significant impact on morbidity and mortality, COVID-19 has become a critical concern in healthcare. Timely detection of the
SARS-CoV-2 virus is crucial. The virus prompts an inflammatory response in the immune system\[6\]. Immune cells, such as macrophages, release pro-inflammatory cytokines, including IL-6 and IL-1β\[7\]. These cytokines activate and recruit other immune cells, thereby strengthening the immune response\[8\]. However, in some cases, an overactive inflammatory response can lead to immune damage and tissue inflammation\[9\]. The role of immune cells in determining the course, severity, and prognosis of COVID-19 is crucial\[10-12\].

Due to its immune response mechanism, COVID-19 affects elderly and immunodeficient patients disproportionately\[13-15\]. Many patients frequently report neurological symptoms\[16, 17\], and studies have consistently linked viral infections to a heightened risk of neurodegenerative diseases\[18-20\]. Therefore, it is plausible to infer an association between COVID-19 and Alzheimer's disease. The association between pre-existing Alzheimer's disease pathology and immune mechanisms may be further strengthened by SARS-CoV-2 infect.

Research has demonstrated that susceptibility to SARS-CoV-2 infection in hosts results in cognitive decline, which is mediated by systemic inflammation\[21\]. Multiple Mendelian randomization studies have indicated a causal relationship between Alzheimer's disease (AD) and COVID-19\[22, 23\]. Some of the same mutated genes have also been found to co-exist in both diseases, such as double mutations in the apolipoprotein E (APOE4) allele\[24-26\]. Additionally, the binding of SARS-CoV-2 viral proteins to host mitochondrial proteins may inhibit oxidative phosphorylation. This process is closely associated with immune cells in COVID-19 patients, and the interaction shows a bias towards age and specific cell types. The pathological process of Alzheimer's disease is closely linked to oxidative phosphorylation. Mitochondrial dysfunction and oxidative stress contribute to neuronal damage and worsening of Alzheimer's disease. Therefore, the pathophysiological processes of both AD and COVID-19 are closely related to oxidative phosphorylation.

To investigate the shared genes and their functions between AD and COVID-19, we analyzed gene chip data from the GEO database. Genes associated with both diseases were identified using differential expression analysis and weighted gene co-expression network analysis (WGCNA) techniques. We then used machine learning methods to identify eight core genes. Additionally, we compared twenty-two immune cell subpopulations in healthy and patient samples using the cibersort method. To enhance comprehension of the link between COVID-19 and AD, we investigated the correlation between the core genes, immune cells, and metabolic pathways. Our results were additionally confirmed through single-cell analysis.

**Results**

**Identification of DEGs**

Based on the GEO database, we obtained datasets for AD and COVID-19. The dataset GSE213313 consists of 45 whole blood samples collected from 34 COVID-19 patients who are either critical or severe,
as well as 11 healthy controls. The samples were obtained using the GPL21185 platform. The *limma* package was utilized to identify DEGs between the two sets of samples. DEGs were defined using the criteria of a *p.value* < 0.05 and |logFC| > 0.585, resulting in the identification of a total of 3587 DEGs, including 1738 up-regulated genes and 1849 down-regulated genes. Similarly, we acquired and integrated the Alzheimer's disease datasets GSE5281 and GSE63060 (based on platforms GPL570 and GPL21185, respectively). Thus, we obtained a sample of 232 Alzheimer's patients and 178 healthy controls. Then 4961 DEGs were identified, consisting of 1869 up-regulated genes and 1738 down-regulated genes. The up- and down-regulated DEGs of the two datasets were intersected separately, resulting in a total of 484 intersected DEGs. Among these, 199 were up-regulated and 285 were down-regulated (Fig. 1A-B).

**Analysis of GO function**

We performed GO enrichment analyses on the common up-regulated and common down-regulated genes obtained above, respectively. The results indicate that the up-regulated genes primarily focus on responses to viral and symbiotic interactions, signaling through cytokines and interferons, and regulation of immune and viral processes (Fig. 1C). And the down-regulated genes are mainly enriched in large subunit of the ribosome and its cytosolic components (Fig. 1D).

**WGCNA**

After removing two outlier samples using a threshold of 140, the remaining samples were analyzed further. To achieve a scale-free network, the *pick Soft Threshold* function of *WGCNA* package was used to sift through power parameters ranging from 1 to 30, ultimately selecting a power of 6 as the soft threshold (Fig. 2A). The identification of 9 modules, each comprising genes that share co-expression profiles, was facilitated by the *cuttree* dynamics and module signature gene function (Fig. 2B). The threshold β was set at 6, and the TOM matrix was used to identify nine gene modules: blue (527), pink (435), red (172), yellow (113), black (132), brown (365), green (743), turquoise (7031), grey (128) (Fig. 2C). The black module shows the correlation between AD and COVID-19 (Fig. 2D-E). The genes in the black module have a positive correlation between the two diseases. The genes in the black module were analyzed for GO enrichment. The results revealed that these genes were associated with pathways such as cytokines, growth factors, apoptosis, response to metal ions, and inorganic substances (Fig. 2F).

**Identification of central genes through machine learning**

By using the random forest algorithm and lasso regression algorithm, we ended up with 8 central genes: ME3, SLC9A6, PCYOX1L, PRR11, GAS2L1, EIF3H, BCL6, TTC19 (Fig. 3A-D). In order to make the screened genes truly valuable in the diagnosis and treatment of diseases, we further evaluated their diagnostic value by making receiver operating characteristic curves (ROC curves). The AUC values of the eight genes mentioned above were as follows: ME3 (0.898), SLC9A6 (0.850), PCYOX1L (0.918), PRR11 (0.850), GAS2L1 (0.855), EIF3H (0.892), BCL6 (0.824), and TTC19 (0.844). The AUC values of the obtained ROC curves were all greater than 0.8, indicating high accuracy and excellent predictive ability of the eight genes mentioned.
Immune cell infiltration and immune cell correlation

We did an immune infiltration analysis of AD versus normal patients and constructed differential expression of immune cells with 8 central genes. In the same way, COVID-19 patients were analyzed. In comparison to normal controls, the AD patient group exhibited upregulation of CD4⁺ naive T cells, regulatory T cells (Tregs), and resting NK cells, while downregulating CD8⁺ T cells and activated NK cells (Fig. 4A). The expression of SLC9A6, EIF3H, and TTC19 showed a negative correlation with the infiltration level of neutrophils, Tregs, and Macrophages M0. BCL6, PRR11, and GAS2L1 were also found to be negatively correlated with CD8⁺ T cells, CD4⁺ memory T cells, memory B cells, and activated NK cells (Fig. 4B). Similarly, CD4⁺ naive T cells, monocytes, macrophages M0, activated mast cells and neutrophils were upregulated and CD8⁺ T cells, CD4⁺ memory resting T cells and resting mast cells were downregulated in the COVID-19 patient group (Fig. 4C). The expression levels of SLC9A6, PCYOX1L, EIF3H, ME3, and TTC19 were found to be negatively correlated with the infiltration levels of activated mast cells, neutrophils, and macrophages M0. BCL6, PRR11, and GAS2L1 were negatively correlated with the infiltration levels of CD8⁺ T cells, CD4⁺ memory T cells, resting mast cells, and resting dendritic cells (Fig. 4D).

To investigate the metabolic pathways of the central genes, we analyzed the correlations between eight central genes and classical metabolic pathways. The genes AD, BCL6, PRR11, and GAS2L1 showed significant positive correlation with hypoxia and significant negative correlation with fatty acid metabolism and oxidative phosphorylation (Fig. 4E). SLC9A6, PCYOX1L, EIF3H, ME3, and TTC19 were found to have a significant positive correlation with fatty acid metabolism and oxidative phosphorylation, as well as a significant negative correlation with hypoxia. Similarly, for COVID-19, BCL6, PRR11, and GAS2L1 showed significant positive correlations with hypoxia, cholesterol homeostasis, xenobiotic metabolism, and glycolysis, and negative correlations with oxidative phosphorylation (Fig. 4F). SLC9A6, PCYOX1L, EIF3H, ME3, and TTC19 were found to have a significant positive correlation with oxidative phosphorylation and a negative correlation with hypoxia, cholesterol homeostasis, xenobiotic metabolism, and glycolysis.

Single-cell data analysis of AD patients

The single cell dataset underwent initial quality checks, assessing correlations among nFeature RNA, nCount RNA, and percent.mt to confirm high-quality cell samples for the study. Figure 5A shows a positive correlation (correlation coefficient = 0.92) between nCount RNA and nFeature RNA, which represent unique molecular identifiers. After excluding some cells, the results are presented in Figures 5B and 5C. The scRNA-seq dataset revealed 3,000 genes exhibiting high variation levels. To further investigate these genes, we identified ten markers that stood out as particularly significant. A principal component analysis (PCA) on the top 20 PCs was performed (Fig. 5D). Following this, the t-SNE and the UMAP algorithms clustered cells into 27 distinct groups (Fig. 6A). The AD group exhibited a decrease in NK cells and an increase in T cell subsets (Fig. 6C). We therefore extracted mainly NK cells and T cells from the AD single cell dataset.
The expression levels of eight core genes were compared in normal subjects and AD patients. In both groups, EIF3H and TTC19 showed higher expression levels, with EIF3H being the most significant (Fig. 6D). Heatmaps display the proportions and the expressions of the eight core genes expressed in immune cells. EIF3H is expressed at a high level in all four immune cell types, both in terms of number and proportion, surpassing the expression levels of other genes (Fig. 7A-B). Furthermore, we suggest an association between the gene EIF3H and oxidative phosphorylation in immune cell subpopulations (Fig. 7C). It is possible that EIF3H plays a role in the oxidative phosphorylation process of immune cells in AD patients.

Materials and Methods

Data download

The gene expression data for AD and COVID-19 was obtained from the GEO database (https://www.ncbi.nlm.nih.gov/geo/). The normal and disease-affected groups were compared using the limma package[27]. The screening criteria for DEGs were a p.value of less than 0.05 and an absolute logFC greater than 0.585. For single-cell correlation analysis, the GSE181279 data file with a total of 5 samples was downloaded.

Enrichment analysis

The R package clusterprofiler was used for annotation and visualization, and the DEGs were analyzed by Gene Ontology (GO) pathway analysis to obtain the biological functions and signaling pathways involved in disease occurrence and development[28]. Enrichment was deemed statistically significant when the p.value < 0.01.

Construction of co-expression networks and identification of hub modules

The R package WGCNA was used to identify genes associated with AD and COVID-19 through a weighted gene co-expression network[29]. To filter out anomalies, a detailed examination was carried out on genes exhibiting expression levels above zero. The construction of the co-expression network leveraged co-expression analysis techniques. Flash clust was utilized for clustering analysis, ensuring network analysis stability by applying this method to each individual sample. Genes sharing similar expression patterns were grouped into modules via the Pearson correlation coefficient, generating a correlation matrix in the process. A soft thresholding approach was then employed to transform this matrix into a weighted adjacency matrix. To pinpoint the modules most pertinent to COVID-19 and AD with precision, the optimal soft threshold was determined, leading to the identification of genes within co-expressed modules.

Feature selection by machine learning
Then, two machine learning algorithms, random forest (RF)\textsuperscript{[30]} and least absolute shrinkage selection (LASSO)\textsuperscript{[31]}, were applied to identify key genes with high diagnostic potential. Random forest is advantageous for data processing of complex, advanced datasets. Using the R package \textit{random forest}, we identified important genes. Genes with importance scores greater than 0.7 were selected. To efficiently screen the genes that contribute the most to disease diagnosis from the set of diagnostic genes selected by RF, we used Lasso regression as an additional screening tool. And we assessed its diagnostic value by plotting the receiver operating characteristic curves (ROC curves).

\textbf{Analysis of immune cell infiltration and immune cell correlation}

The CIBERSORT algorithm was employed to evaluate the type and content of immune cells in the samples\textsuperscript{[32]}. The CIBERSORT algorithm is a computational method developed to deconvolute the cell composition of complex tissues from their gene expression profiles. This algorithm incorporates 22 immune cell types, including T cells, B cells, monocytes, M1 and M2 macrophages, natural killer (NK) cells, and others. The CIBERSORT algorithm was used to estimate the cell type in the sample using the genetic information obtained from the tissue sample. And the relationship between immune cells and central genes in AD and COVID-19 was constructed.

\textbf{Single-cell data analysis}

For the GSE181279 dataset, we utilized the \textit{seurat} package for PCA and t-SNE analyses, excluding cells based on feature and mitochondrial gene counts\textsuperscript{[33]}. We normalized gene expression using \textit{LogNormalize} and identified 3,000 HVGs with the \textit{vst} method. We determined significant PCs through PCA and used the elbow method, then applied t-SNE on 20 PCs. Cells were grouped into 27 clusters and DEGs were identified to ascertain cell types using \textit{SingleR} with \textit{HumanPrimaryCellAtlasData} as the reference\textsuperscript{[34, 35]}. Finally, hub gene expression was showcased in immune cells using violin diagrams. Subsequently, the relationship between immune cells and metabolism in both AD and COVID-19 was examined using Pearson correlation in the \textit{stats} package of the R language.

\textbf{Discussion}

In recent years, bioinformatics has rapidly developed, providing technical and methodological support for utilizing database information. This has made it possible to explore the pathophysiological links between AD and COVID-19 using public databases. Infection with the SARS-CoV-2 virus triggers an immune response in the body\textsuperscript{[36, 37]}. In some patients, this can lead to a cytokine storm, causing an excessive immune response\textsuperscript{[38, 39]}. Alzheimer's disease is characterized by dysregulation of the immune system, and the immune system is involved in the pathophysiological mechanisms of the disease\textsuperscript{[40-42]}. As diseases closely related to the immune system, both Alzheimer's disease and COVID-19 have been extensively studied. The association between Alzheimer's disease and COVID-19 is currently of interest due to compelling evidence from multiple studies supporting the link.
Research has demonstrated a significant correlation between genetic risk for Alzheimer's disease and susceptibility to severe COVID-19, which is strongly associated with an inflammatory response\cite{43}. Additionally, Mendelian randomization studies have suggested a causal relationship between Alzheimer's disease and COVID-19\cite{44,45}. According to a study, individuals with pre-existing cognitive impairment may be at a higher risk of SARS-CoV-2 virus infection and may experience a more severe prognosis after COVID-19 infection compared to those with normal cognitive function\cite{46}. The combination of WGCNA and machine learning approaches allowed us to identify key genes shared by AD and COVID-19. This facilitates the identification of patients in the early stages of the disease. Additionally, ssGSEA was used to assess the role of oxidative phosphorylation in the immunity of AD, further elucidating its inflammatory levels and pathological processes.

Numerous studies have explored the correlation between AD and COVID-19. However, there is a scarcity of comprehensive research on the shared genes, metabolic pathways, and immune cells between the two diseases. By utilizing WGCNA to identify common modules, we have discovered the core black module, which exhibits the highest degree of association with both diseases. Through GO enrichment analysis, it is evident that the genes are centrally enriched in pathways related to the cellular response to metal ions. This is significant as the accumulation of metal ions in the brain is closely linked to the progression of AD\cite{47}. Deposition of metal ions in various brain regions impairs mitochondrial function, leading to oxidative stress and a range of pathological responses\cite{48,49}. Excessive intracellular accumulation of zinc can induce toxicity through various mechanisms, such as increasing ROS production by disrupting mitochondrial function and exacerbating neuronal death\cite{47}. In AD patients, increased copper deposition has been observed\cite{50}.

Copper can interact with Aβ and tau proteins, promoting pathological aggregation and deposition of these proteins\cite{50}. Additionally, serum zinc ion levels may significantly affect antibody responses in COVID-19 patients\cite{51}. In vitro experiments have demonstrated that zinc ions inhibit SARS-CoV-2 major proteases and viral replication\cite{52}. Severe COVID-19 is more likely to develop in patients with severe zinc deficiency, and this effect may be mediated by the binding of zinc ions to ACE2, thereby affecting the binding affinity of SARS-CoV-2 to the receptor molecule\cite{53-56}. The effect of copper ions on COVID-19 has also received much attention\cite{55}. Research has demonstrated that copper ions in COVID-19 patients contribute to the overproduction of reactive oxygen species (ROS), which is a significant factor in the development of lung injury\cite{57}. Therefore, both zinc and copper ions play a role in the pathological process of AD and COVID-19, and are closely linked to oxidative stress and oxidative phosphorylation. Additionally, the literature suggests that cadmium ions may play a role in the pathological process of AD\cite{58,59}.

These studies support our findings. However, there is limited research on the association between cadmium ions and COVID-19. It is speculated that cadmium ions may also be involved in the pathophysiology of COVID-19, potentially through pathways such as oxidative phosphorylation and oxidative stress. However, further experiments will be necessary for confirmation.
This study investigates the shared biomarkers between AD and COVID-19. Two machine learning techniques, RF and LASSO, were used to select eight genes with co-diagnostic value: ME3, SLC9A6, PCYOX1L, PRR11, GAS2L1, EIF3H, BCL6, and TTC19. The effectiveness of these genes as diagnostic tools was validated by analyzing their ROC curves. Furthermore, after conducting a thorough analysis of immune penetration and metabolic pathways, it was discovered that these diagnostic genes exhibited significant expression levels in various immune cell subtypes and metabolic pathways. Notably, during the examination of single-cell data for Alzheimer's disease, the EIF3H gene was observed to be highly expressed in multiple immune cell subtypes.

The gene EIF3H encodes a subunit of the eukaryotic translation initiation factor 3 (eIF3) complex\(^\text{[60]}\). This complex is crucial in the initiation phase of protein synthesis. EIF3H plays a significant role in facilitating the early steps of protein synthesis as part of one of the largest and most complex initiation factors\(^\text{[60]}\). Studies have demonstrated that EIF3H exhibits modified expression in certain cancer diseases, which correlates with oxidative phosphorylation\(^\text{[61]}\). Additionally, a possible association between eIF3h and oxidative stress has been suggested\(^\text{[62]}\). It has been shown in several studies that EIF3H is associated with viral infectious diseases, including rabies virus and hepatitis C virus (HCV)\(^\text{[63, 64]}\). Through metabolic analyses of AD and COVID-19, a relationship between core genes and oxidative phosphorylation has been identified. EIF3H was found to be strongly associated with oxidative phosphorylation in both diseases, as confirmed by single cell analysis in AD.

During our analysis of AD and COVID-19, we identified a clear correlation in the oxidative phosphorylation pathway among certain core genes. Our results suggest that these genes may have a significant role in the development of these diseases. However, there is limited research on the gene EIF3H in relation to these diseases, and our findings should be considered preliminary. Further experiments are necessary to confirm our results.

Using WGCNA and machine learning methods, we screened 8 core genes. We then conducted immune infiltration analysis for two diseases and analyzed the relationship between the core genes, immune cells, and metabolic pathways. These findings have implications for the diagnosis of AD and COVID-19, and provide guidelines for further investigation into the link between these two diseases in terms of pathogenesis. However, this study has limitations, and further animal experiments are necessary to support our findings. Our future work will involve constructing animal models and using gene knockdown and other experimental methods to improve the study.

**Conclusion**

This research uncovers shared genetic markers, signaling mechanisms, immune system modifications, and alterations in metabolic pathways that may collectively contribute to the development of both COVID-19 and Alzheimer's disease. By exploring these shared factors, researchers can gain a deeper understanding of the complex interplay between the two conditions. Additionally, identifying these shared factors creates new opportunities for diagnosing and treating both diseases. By focusing on these
shared factors, researchers may potentially discover new methods to combat both COVID-19 and Alzheimer's disease, ultimately enhancing patient outcomes and quality of life.

**Declarations**

**Data Availability Statement**

Publicly available datasets were analyzed in this study.

**Ethical approval and consent to participate**

The research analyzed public anonymous data and human subjects review was not required.

**Consent for publication**

All authors approved the final manuscript and the submission to this journal.

**Availability of data and material**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Competing Interest**

The authors disclosed no conflicts of interest.

**Author contributions**

Jun Liu and Juntu Li conceived and designed the study. Juntu Li and Yanyou Zhou collected and analyzed the data. Juntu Li, Yanyou Zhou, Linfeng Tao, Yue Zhu, Chao Li, Yiyuan Pan and Jun Liu wrote the paper. All the authors contributed to the article and approved the submitted version.

**Funding**

This study was supported by the Key Social Development Project of Jiangsu Province (BE2021660), Key R&D Plan Projects in Kunshan City (KSF202105) and Suzhou Science and Technology Project (SKY2023197).

**References**


Figures
Figure 1

Differential analysis and KEGG enrichment analysis of AD and COVID-19 patients (A) Intersection of DEGs upregulated by AD and COVID-19 (B) Intersection of DEGs downregulated by AD and COVID-19 (C) GO enrichment analysis for common upregulated genes (D) GO enrichment analysis for common downregulated genes
Figure 2

Co-expression modules and enrichment analysis in patients with AD and COVID-19 (A) Analysis of the network topology of soft threshold power (B) Cluster dendrogram identifying co-expressed genes (C) The module–trait relationships in AD and COVID-19. Correlations and p-values are provided for each module (D) Correlation of black modules with AD (E) Correlation of black modules with COVID-19 (F) GO enrichment analysis for black module genes
Figure 3

Co-Diagnostic Gene Screening and Machine Learning Modelling (A) Relationship between the number of decision trees and the error rate. Green nodes represent root nodes, black nodes represent non-leaf nodes and red leaf nodes represent classification results (B) The random forest method was used to screen the top 30 candidate genes. The horizontal coordinates indicate the gene importance coefficients, while the vertical coordinates show the gene names. (C) Spectrum of Lasso coefficients for candidate genes (D) Optimal Tuning Parameter Evaluation for LASSO Regression with Cross-Validation
Figure 4

Immune cells and metabolic pathways in patients with AD and COVID-19 (A) Infiltration of immune cells between AD and healthy samples (B) Immune infiltration analysis of 8 candidate genes in AD (C) Infiltration of immune cells between COVID-19 and healthy samples (D) Immune infiltration analysis of 8 candidate genes in COVID-19 (E) Correlation between the expression levels of seven hub genes and the ssGSEA enrichment scores for classical metabolic pathways in the AD data (F) Correlation between the expression levels of seven hub genes and the ssGSEA enrichment scores for classical metabolic pathways in the COVID-19 data. *p < 0.05, **p < 0.01, ****p < 0.001.
Figure 5

Process for quality control of single-cell data. (A) The relationship among gene expression, cell counts, and mitochondrial content within individual samples. (B) Percentage of mitochondrial genes (mt), RNA features (nFeatureRNA), and RNA counts (nCountRNA) for each sample prior to filtration. (C) Percentage of mitochondrial genes (mt), RNA features (nFeatureRNA), and RNA counts (nCountRNA) for each sample.
Single-cell subpopulation identification and expression levels of genes in AD patients and normal controls (A) TSNE visualization illustrating cell subpopulations in patients with Alzheimer's Disease (AD). (B) UMAP visualization illustrating cell subpopulations in patients with Alzheimer's Disease (AD). (C) Ratio of immune cell composition in AD patients to normal subjects (D) Comparison of expression levels of core genes.
Figure 7

Co-localisation and differential expression of core genes in immune cells of AD patients (A) Proportion of core gene expression in immune cells of AD patients and normal subjects (B) Core gene expression in immune cells of AD patients and normal subjects (C) Co-localisation of oxidative phosphorylation metabolic pathways and EIF3H in AD patients and healthy subjects.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.
- Sup1.png
- Sup2.png