Comprehensive bioinformatic analysis of the expression and prognostic significance of TSC22D domain family genes in acute myeloid leukemia

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Abstract

Background:

TSC22D domain family genes, including TSC22D1-4, have been extensively reported to be involved in tumors. However, their expression profiles and prognostic significance in acute myeloid leukemia (AML) remain unknown.

Methods:

The present study investigated the expression profiles and prognostic significance of TSC22D domain family genes in AML through the use of multiple online databases, including the CCLE, EMBL-EBI, HPA, Oncomine,GEPIA2, UALCAN, BloodSpot, and GSCALite databases. The cBioPortal and GSCALite databases were used to explore the genetic alteration and copy number variation (CNV) of TSC22D3. TRRUST Version 2 was used to explore the gene ontology biological process, disease ontology, and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways associated with TSC22D3. The AnimalTFDB3.0, STRING, and Harmonizome databases were used to investigate the protein–protein interaction (PPI) network of TSC22D3. Harmonizome was used for TSC22D gene regulatory kinase analysis. The TargetScanHuman 8.0, MiRDB, and ENCORI databases were used to execute the analysis of TSC22D3 regulatory miRNAs. Then, the GSCALite and GEPIA2021 databases were used to investigate the correlation between TSC22D3 expression and immune infiltration.

Results:

The expression of TSC22D3 was upregulated markedly in AML cells relative to normal hematopoietic stem cells. The expression of TSC22D3 was increased in AML group compared with normal control group. And overexpression of TSC22D3 was associated with poor OS in AML patients.Furthermore, gene ontology analysis revealed that TSC22D3 was involved in leukemia. Functional enrichment analysis indicated that TSC22D3 has many biological functions, including the regulation of many genes, kinases, miRNAs, signaling pathways, and immune infiltration.

Conclusions:

TSC22D3 expression was upregulated in AML, and overexpression was associated with poor OS in AML patients. Therefore, TSC22D3 may serve as a novel prognostic biomarker for AML.

INTRODUCTION

Acute myeloid leukemia (AML) is an aggressive hematopoietic malignancy with high biological and clinical heterogeneity[1]. Despite advances made in the diagnosis and treatment of AML, the increased risk of relapse and low 5-year survival rate after diagnosis remain significant challenges[2]. Authentication of new AML biomarkers can help to clarify the pathogenesis of the disease and guide the diagnosis, treatment, and prognosis evaluation of AML[3]. TSC22D domain family genes have been

extensively reported to play an essential role in tumors[4-8]. Nonetheless, their expression profiles and prognosis in AML remain unclear. Herein, we conducted an analysis of the expression and prognostic value of TSC22D domain family genes in AML through the use of multiple online databases. See Supplementary Material 1 for the details of each online database login site.

MATERIALS AND METHODS

Gene expression analysis

Analysis of gene expression of the TSC22D domain family in AML cell lines

Cancer Cell Line Encyclopedia (CCLE) is a multiomics online database collection of 1378 cell lines[9]. The expression data of TSC22D domain family genes in forty-four AML cell lines was downloaded from Expression 21Q4 Public dataset in the CCLE database (Supplementary Material 2) and then used by the cluster heatmap tool from the website (http://www.bioinformatics.com.cn) for visualization.

EMBL-EBI is an integrated bioinformatics research database[10].The data and figures related to gene expression of the TSC22D domain family in fourteen AML cell lines were downloaded from Expression Atlas dataset in the EMBL-EBI database (Supplementary Material 3).

Human Protein Atlas (HPA) is a comprehensive database of proteomics, transcriptomics, and systems biology data[11]. The pictures of gene expression of the TSC22D domain family in five AML cell lines were downloaded from the HPA database.

Analysis of gene expression of the TSC22D domain family in AML cells and normal hematopoietic stem cells

Oncomine is the world's largest database of oncogene chips and integrated data mining platforms [12]. Data of gene expression of the TSC22D domain family in AML cells and CD34-positive peripheral blood cells was downloaded from the Valk leukemia dataset[13] in the Oncomine database and then used by GraphPad Prism 8 for statistical analysis (Supplementary Material 4).

BloodSpot is an online open data platform with data from the Cancer Genome Atlas (TCGA) and Gene Expression Omnibus (GEO) databases that provides gene expression profiles and gene traits in healthy and malignant hematopoiesis, as well as Kaplan–Meier survival maps[14] . Data of gene expression of the TSC22D domain family in AML cells and normal hematopoietic stem cells was downloaded from the normal hematopoiesis with AML dataset (Supplementary Material 5) and the blood- pool AML samples with normal cells dataset (Supplementary Material 6) in the BloodSpot database. Then the expression data was used by GraphPad Prism 8 for statistical analysis.

Analysis of gene expression of the TSC22D domain family in AML group and normal control group

The expression pictures of the TSC22D domain family genes in AML tissues and healthy bone marrow were downloaded from the Valk leukemia dataset in the Oncomine database.

GEPIA2 is an updated and enhanced online publicly accessible database based on TCGA and Genotype-Tissue Expression (GTEx) databases for tumor and normal samples for gene expression analysis[15] .The pictures of gene expression of the TSC22D domain family in AML tissues and normal tissues were downloaded from the GEPIA2 database.

Data of the TSC22D domain family genes in AML tissues and healthy bone marrow samples was downloaded from the Leukemia MILE Study dataset (GSE13159) in the BloodSpot database (Supplementary Material 7) and used by GraphPad Prism 8 for statistical analysis.

Survival analysis

UALCAN is an online, accessible, and interactive network resource for cancer omics data analysis[16] .

GSCALite is an open, online, web-based platform for genomic cancer analysis[17].

The pictures of the effect of the TSC22D domain family gene expression on AML patient survival were downloaded from the GEPIA2, UALCAN, BloodSpot, and GSCALite databases.

Genetic alteration and copy number variation (CNV) analysis of TSC22D3

cBioPortal is a public database to interactively explore multidimensional genomic datasets of cancers[18]. The figures related to the genetic alterations and the survival data of AML patients grouped according to TSC22D3 expression were downloaded from the TCGA PanCancer dataset in the cBioPortal database.

The pictures of the CNV summary and survival analysis of TSC22D3 in AML were downloaded from the GSCALite database.

Functional enrichment analysis of TSC22D3

TRRUST Version 2 is an online, open database of human and mouse transcriptional regulatory networks[19] .

The gene ontology biological process, disease ontology, and KEGG pathway data associated with human TSC22D3 transcription factor (TF) were downloaded from TRRUST Version 2 (Supplementary Material 8) and then used by the bar with a color gredient tool from the website(http://www.bioinformatics.com.cn) for visualization.

Protein–protein interaction (PPI) analysis of TSC22D3

AnimalTFDB3.0 is an online database aimed at providing the most comprehensive and accurate information for animal (including human) TFs and cofactors[20].

STRING is an online open database aimed at providing customized protein–protein networks[21] .

The pictures of the PPI analysis of TSC22D3 were downloaded from the AnimalTFDB3.0 and STRING database.

Harmonizome is an online database of processed datasets of gene and protein knowledge from more than 70 major online sources[22]. Data of PPI analysis of TSC22D3 was downloaded from the Harmonizome database (Supplementary Material 9) and then used by Cytoscape[23] analysis software to visualize the results.

Analysis of TSC22D3 regulated kinases

Data of the predicted TSC22D3 kinase interactions was downloaded from the Harmonizome database (Supplementary Material 10) and used by the circular heatmap tool from the website (http://www.bioinformatics.com.cn) for visualization.

Analysis of TSC22D3 regulated miRNAs

TargetScanHuman 8.0 is an online database that predicts relationships between human miRNAs and target genes[24]. Data of the conserved miRNA families of TSC22D3 was downloaded from the TargetScanHuman 8.0 database (Supplementary Material 11) and then used by the flower plot tool from the website (http://www.bioinformatics.com.cn) for visualization.

MiRDB is an online database for the prediction of miRNA target genes[25] .

Data of the predicted miRNAs of TSC22D3 was downloaded from the miRDB database (Supplementary Material 12) and then used by the flower plot tool from the website (http://www.bioinformatics.com.cn) for visualization.

The Encyclopedia of RNA Interactomes (ENCORI) is an online open source platform for studying data on RNA interactions[26] .

Data of the predicted miRNAs of TSC22D3 was downloaded from the ENCORI database (Supplementary Material 13) and used by Cytoscape analysis software to visualize the results.

Immune infiltration analysis of TSC22D3

Data of the correlation between the TSC22D3 expression and immune infiltration in AML wasdownloaded from the GSCALite database (Supplementary Material 14) and used by the correlation coefficient analysis tool from the website (http://www.bioinformatics.com.cn) for visualization.

GEPIA2021 is an online database for tumor immune invasion analysis[27].The CIBERSORT algorithm was used to explore the correlation between TSC22D3 expression and immune infiltration in AML.

RESULTS

Comprehensive bioinformatics analysis of the TSC22D domain family genes in AML was performed by using data from TCGA and GEO databases. The specific analysis process is shown in Figure 1.

Analysis of gene expression of the TSC22D domain family in AML cell lines, normal hematopoietic stem cells, AML tissues and healthy bone marrow

First of all, three different databases, including the CCLE, EMBL-EBI, and HPA databases, were used to authenticate the expression of the TSC22D domain family genes in AML cell lines. The results showed that TSC22D domain family genes were abnormally expressed in AML cell lines at different levels (Figure 2). Secondly, the Oncomine and BloodSpot databases were used to check the expression of TSC22D domain family genes in AML cells and normal hematopoietic stem cells. These data from TCGA and GEO databases revealed that the expression of TSC22D3 was upregulated markedly in AML cells relative to normal hematopoietic stem cells, whereas the expression of TSC22D1 was the opposite

(Figure 3). As depicted in Figure 4, analysis from the Oncomine and GEPIA2 databases revealed that the expression of TSC22D1 and TSC22D3 was upregulated markedly in AML tumor samples compared with healthy bone marrow samples(Figure 4a, 4b). Meanwhile, a large sample data from GSE13159 in the BloodSpot database further confirmed this conclusion(Figure 4c).

Survival analysis according to the expression of the TSC22D domain family genes in AML

High expression of TSC22D3 was associated with poor OS in AML patients by survival analysis of the GEPIA2, UALCAN, BloodSpot, and GSCALite databases (Figure 5).

Genetic alteration and CNV analysis of TSC22D3

Analysis of the TCGA PanCancer Atlas dataset from the cBioPortal database revealed that the mutation rate of the TSC22D3 gene was 8%, and TSC22D3 gene alteration did not affect the OS of AML patients. Likewise, CNV analysis of the GSCALite database showed that the incidence of CNV of the TSC22D3 gene was low in AML and did not affect the OS of AML patients (Figure 6).

Functional enrichment analysis of TSC22D3

The gene ontology biological processes, disease ontology terms and KEGG pathways associated with TSC22D3 were analyzed by using the TRRUST database. The results showed that TSC22D3 has many biological functions (Figure 7A). Disease ontology analysis revealed that TSC22D3 was involved in tumors, including leukemia (Figure 7B). Furthermore, KEGG pathway analysis indicated that TSC22D3 was involved in the regulation of multiple signaling pathways (Figure 7C).

PPI analysis of TSC22D3

PPI analysis from the AnimalTFDB3.0, STRING, and Harmonizome databases indicated that the TSC22D3 protein interacted with many proteins related to the regulation of cell proliferation and differentiation, including FOS, JUN, and NFkB, etc. (Figure 8A, 8B, 8C).

Analysis of kinases regulated by TSC22D3

The Top20 predicted kinases regulated by TSC22D3 through the use of the Harmonizome database revealed that TSC22D3 regulated many kinases, including MAP4K1,MAP2K2, MAP2K3, BCKDK, MYLY,TYK2,and STK10. These kinases are associated with poor OS in AML. (Figure 9).

Analysis of miRNAs regulated by TSC22D3

Analysis of TSC22D3 regulated miRNAs from the TargetScanHuman 8.0, MiRDB, and ENCORI databases indicated that TSC22D3 regulated many miRNAs, including hsa-miR-101-3p, hsa-miR-125b-5p, hsa-miR-135b-5p, hsa-miR-182-5p, hsa-miR-193a-3p, hsa-miR-216b-5p, hsa-miR-362-5p, hsa-miR-370-3p, and hsa-miR-98-5p, etc. (Figure 10).

Immune infiltration analysis of TSC22D3

Analysis of TSC22D3 gene expression and immune infiltration in AML from the GSCALite database indicated that TSC22D3 was enriched in exhausted T cells, macrophages and monocytes. Analysis of TSC22D3 gene expression and immune infiltration in AML samples from the GEPIA2021 database

revealed that TSC22D3 was enriched in resting memory CD4+ T cells, CD8+ T cells, resting NK cells, plasma cells, monocytes, etc. (Figure 11).

DISCUSSION

TSC22D domain family genes, including TSC22D1-4, belong to the leucine zipper TF family and have been reported to be involved in regulating cell proliferation and differentiation[28]. TSC22D1, also called transforming growth factor-β-stimulated clone-22, was reported to play a tumor suppressor role in tumors[29]. TSC22D2 overexpression depends on the TSC22D2-PKM2-CyclinD1 regulatory axis to inhibit tumor cell growth in colorectal cancer[30]. TSC22D3, also known as glucocorticoid-induced leucine zipper (GILZ), can promote or suppress tumor growth, depending on the type of tumor and its microenvironment. TSC22D3 plays a dual role in tumors: it not only exerts a tumor-promoting effect by influencing the immune system and tumor microenvironment but also inhibits tumor growth by inducing apoptosis or suppressing the proliferation of cancer cells[31]. TSC22D4, also known as THG-1, was reported to promote esophageal squamous cell carcinoma cell tumorsphere growth[32]. However, the expression of TSC22D domain family genes and their prognostic value in AML remain unclear.

The present study examined the expression profiles and prognostic significance of TSC22D1-4 genes in AML using multiple online databases. Our study indicated that TSC22D domain family genes were abnormally expressed in AML cell lines at different levels. The expression of TSC22D3 was markedly upregulated in AML cells relative to normal hematopoietic stem cells, whereas the expression pattern of TSC22D1 was the opposite. Furthermore, the expression of TSC22D1 and TSC22D3 increased in AML tumor samples compared with healthy bone marrow samples. Further survival analysis revealed that high expression of TSC22D3 resulted in poor OS in AML patients.Therefore, we identified TSC22D3 as a new prognostic biomarker for AML. Next, analysis of the profiles of the alteration and CNV of TSC22D3 in AML revealed that the incidence of genetic alterations and CNV of TSC22D3 were low in AML and did not affect the OS of AML patients.

As a TF, TSC22D3 is involved in regulating TF activity and signaling pathways. TSC22D3 promotes tumor growth by downregulating the antiapoptotic protein MCL[33]. TSC22D3 confers leukemia cells with a proliferative and metabolic advantage by reprogramming glycolytic metabolism in tumor cells[34]. Hence, we analyzed the gene ontology biological process, disease ontology terms, and KEGG pathways associated with the human TSC22D3 TF using TRRUST Version 2. Our study indicated that TSC22D3 had many biological functions, including the response to DNA damage stimulus, the regulation of cell proliferation , cell cycle arrest, and etc. Disease ontology analysis revealed that TSC22D3 was involved in leukemia. Furthermore, KEGG pathway analysis indicated that TSC22D3 was involved in regulating multiple signaling pathways, including the FoxO signaling pathway, AMPK signaling pathway, PI3K−Akt signaling pathway, JAK−STAT signaling pathway, etc. These signaling pathways play a part in cancer progression. PPI analysis indicated that TSC22D3 proteins interact with many proteins, including FOS, JUN, NFkB, and etc, which are involved in regulating the proliferation and differentiation of tumor cells. TSC22D3 promoted tumor cell proliferation by regulating AKT kinase[35]. Therefore, we analyzed the Top

20 kinases regulated by TSC22D3 TF, including MAP4K1,MAP2K2, MAP2K3, BCKDK, MYLY,TYK2,and STK10. These kinases are associated with poor OS in AML.And these kinases are involved in various cellular activities, such as cell proliferation and differentiation, etc. Furthermore, we analyzed the TSC22D3 regulated miRNAs. The results revealed that TSC22D3 regulated many miRNAs, including hsa-miR-101-3p, hsa-miR-125b-5p, hsa-miR-135b-5p, hsa-miR-182-5p, hsa-miR-193a-3p, hsa-miR-216b-5p, hsa-miR-362-5p, hsa-miR-370-3p, hsa-miR-98-5p, and etc. These miRNAs were reported to participate in the occurrence and development of AML[36].

TSC22D3 has been reported to be involved in the supervision of the cell cycle, differentiation, and apoptosis of immune cells[37]. TSC22D3 can play an anti-inflammatory and immunosuppressive role in tumor development. Activation of the immunosuppressive TSC22D3 TF in dendritic cells can result in treatment failure[38]. TSC22D3 upregulation can subvert therapy-induced anticancer immuno-

surveillance[39]. As a TF, TSC22D3 can mediate the immunosuppressive and anti-inflammatory effects of T cells and macrophages by inhibiting nuclear factor-κB (NF-κB)-dependent transcription[40, 41]. Furthermore, TSC22D3 can play a significant role in tumor progression by mediating the increase in cell quantity and activity of Treg cells through the TGF-β signaling pathway[42, 43]. TSC22D3 could play an indispensable role in the tumor microenvironment by influencing all immune system cells that infiltrate the tumor microenvironment[44]. In addition, TSC22D3 could serve as a pivotal regulator of T cell predysfunction[45]. Recent research shows that the proliferation, survival, and drug resistance of AML cells are sustained and modulated by the bone marrow immunosuppressive microenvironment[46]. Hence, we conducted an analysis of TSC22D3 expression and immune infiltration in AML. The results indicated that the TSC22D3 gene was enriched in exhausted T cells, CD8+ T cells, macrophages and monocytes, etc.

Conclusions

TSC22D3 expression was upregulated in AML, and overexpression was associated with poor OS in AML patients.Therefore, TSC22D3 may serve as a new prognostic biomarker for AML. TSC22D3 may be involved in AML through multiple mechanisms, including the regulation of genes, kinases, miRNAs, signaling pathways and immune infiltration. However, the specific mechanism of TSC22D3 in AML progression still needs to be further studied.

Abbreviations

acute myeloid leukemia : AML; Cancer Cell Line Encyclopedia: CCLE;copy number variation: CNV; Kyoto Encyclopedia of Genes and Genomes: KEGG; Human Protein Atlas: HPA; Cancer Genome Atlas: TCGA; Gene Expression Omnibus: GEO; Genotype-Tissue Expression: GTEx; transcription factor: TF; protein–protein interaction : PPI;Encyclopedia of RNA Interactomes: ENCORI; glucocorticoid-induced leucine zipper : GILZ.

Declarations

Ethics approval and consent to participate

TCGA and GEO belong to public databases. The patients involved in the database have obtained ethical approval. Users can download relevant data for free for research and publish relevant articles. Our study is based on open source data, so there are no ethical issues and other conflicts of interest. And this study was approved by the Academic Committee of First Center Clinic College of Tianjin Medical University and conducted according to the principles expressed in the Declaration of Helsinki.

Consent for publication

Not applicable

Availability of data and materials

The datasets provided for this study can be found and accessed in online databases. These data are also provided in the Supplementary Materials. The login sites of online databases in our study are as follows. CCLE(https://www.broadinstitute.org/ccle) ;EMBL-EBI(https://www.ebi.ac.uk);HPA(https://

www.proteinatlas.org);GEPIA2(http://gepia2.cancer-pku.cn/);GEPIA2021(http://gepia2021.cancer-pku.cn/) ; UALCAN(http://ualcan.path.uab.edu/);BloodSpot(http://servers.binf.ku.dk/bloodspot/) ;

cBioportal(https://www.cbioportal.org); GSCALite (http://bioinfo.life.hust.edu.cn/web/GSCALite/) ; String(https://string-db.org) ; TargetScan8.0(http://www.targetscan.org/) ; MiRDB

(http://www.mirdb.org/) ; ENCORI(https://starbase.sysu.edu.cn/) ; TRRUST Version 2

(http://www.grnpedia.org/trrust/) ; AnimalTFDB3.0 (http://bioinfo.life.hust.edu.cn/HumanTFDB/) ; Harmonizome(http://amp.pharm.mssm.edu/Harmonizome) . Although Oncomine database had been offline, data from Oncomine database was available in the Supplementary Materials and objectively real.

Competing interests

All authors declare that there are no competing interests.

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Authors' contributions

XQX: conceptualization, data analysis, and writing; XJ and JXW: data analysis, and writing; RS, MZ, XX, DNX: editing the article; MFZ: supervision of the project and reviewing, writing, and editing of the article. All authors revised the article.

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Figures

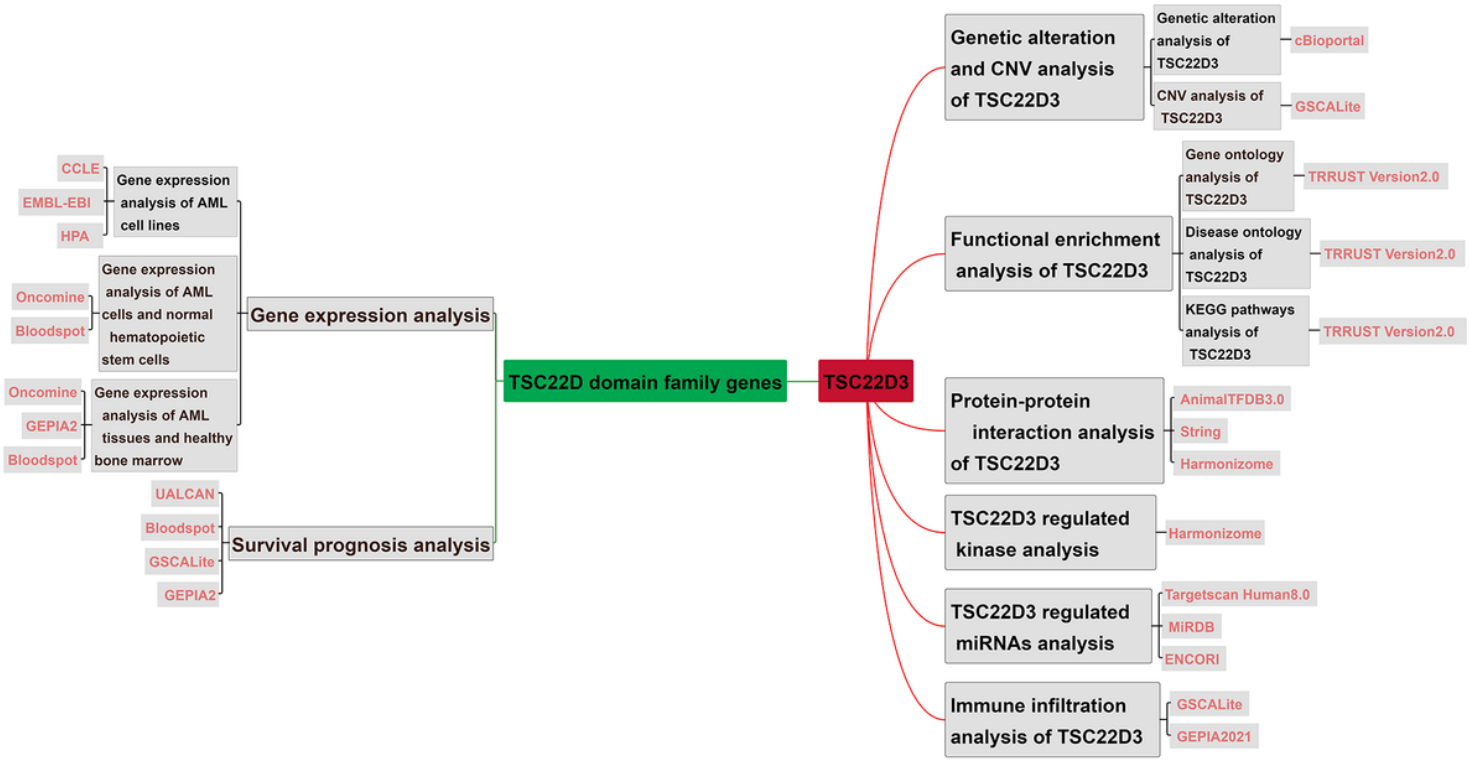

Figure 1 A mind map of the present study.Data was obtained from TCGA and GEO databases to analyze the expression and prognosis of the TSC22D domain family genes in AML.

Figure 1

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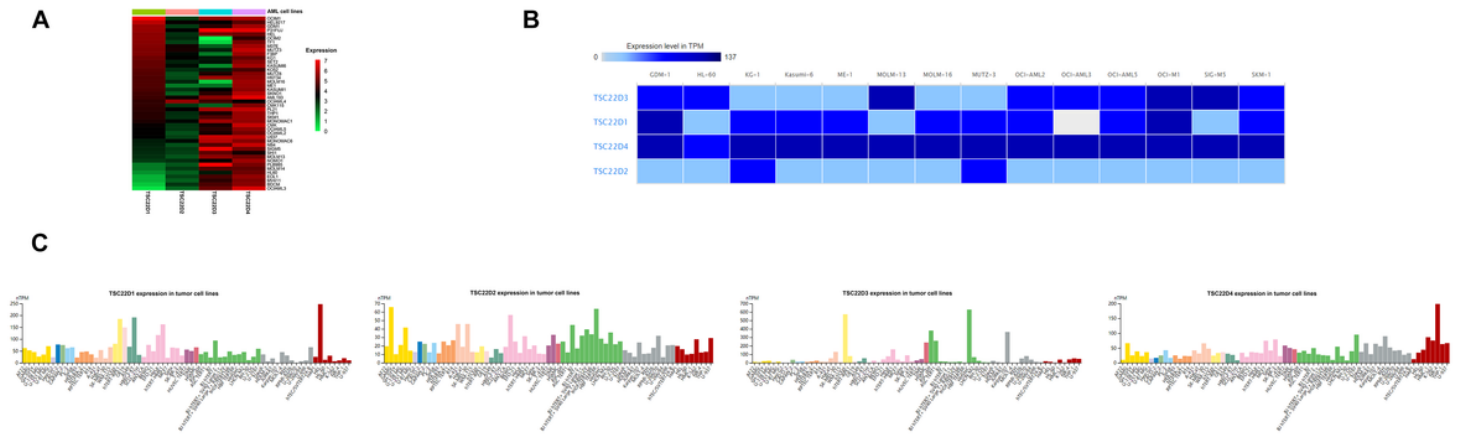

Figure 2 Gene expression of the TSC22D domain family in AML cell lines. **(A)**Heatmap of the expression of the TSC22D domain family genes in 44 AML cell lines in the CCLE database. The color of the Heatmap represented the level of gene expression. **(B)** Bar chart of the expression of the TSC22D domain family genes in 14 AML cell lines in the EMBL-EBI database.The shade of color in the bar graphs indicated the level of gene expression. **(C)** Bar graphs of the expression of the TSC22D domain family genes in human cancers (including 5 AML cell lines) in the HPA database.The height of the bar charts represented the level of gene expression.

Figure 2

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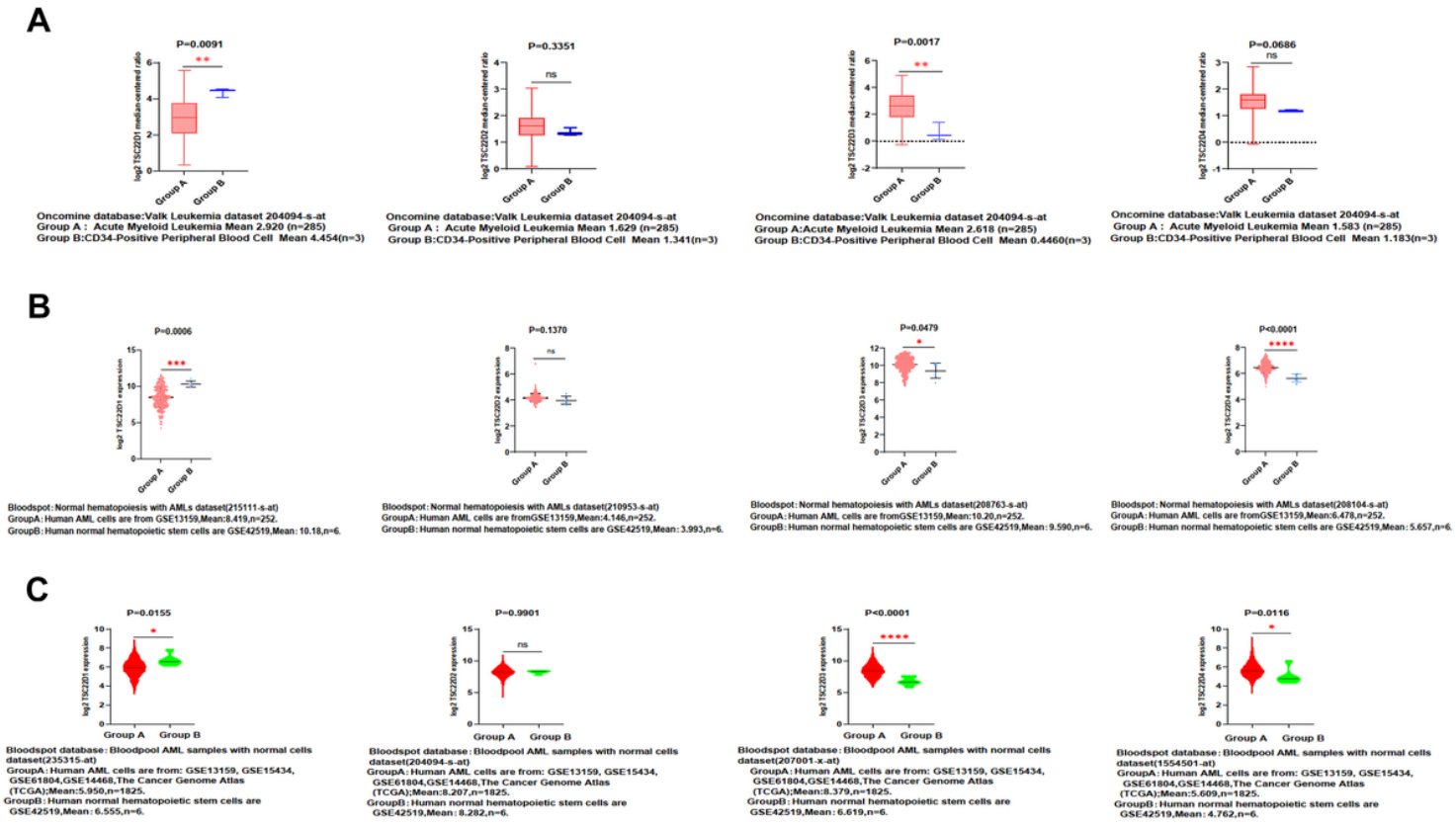

Figure 3. Gene expression analysis of the TSC22D domain family in the normal hematopoiesis and AML cells. **(A)** Boxplots displayed the expression of the TSC22D domain family genes in the Valk Leukemia dataset from the Oncomine database.**(B)**Treemaps displayed the expression of the TSC22D domain family genes from GEO in the normal hematopoietic and AMLs datasets of the Bloodspot database.**(C)** Violin diagrams displayed the expression of the TSC22D domain family genes from TCGA and GEO in the Bloodpool AML samples with normal cells dataset of the Bloodspot database.(*P<0.05, **P<0.01, ***P<0.001,****P<0.0001,ns means no statistical significance).

Figure 3

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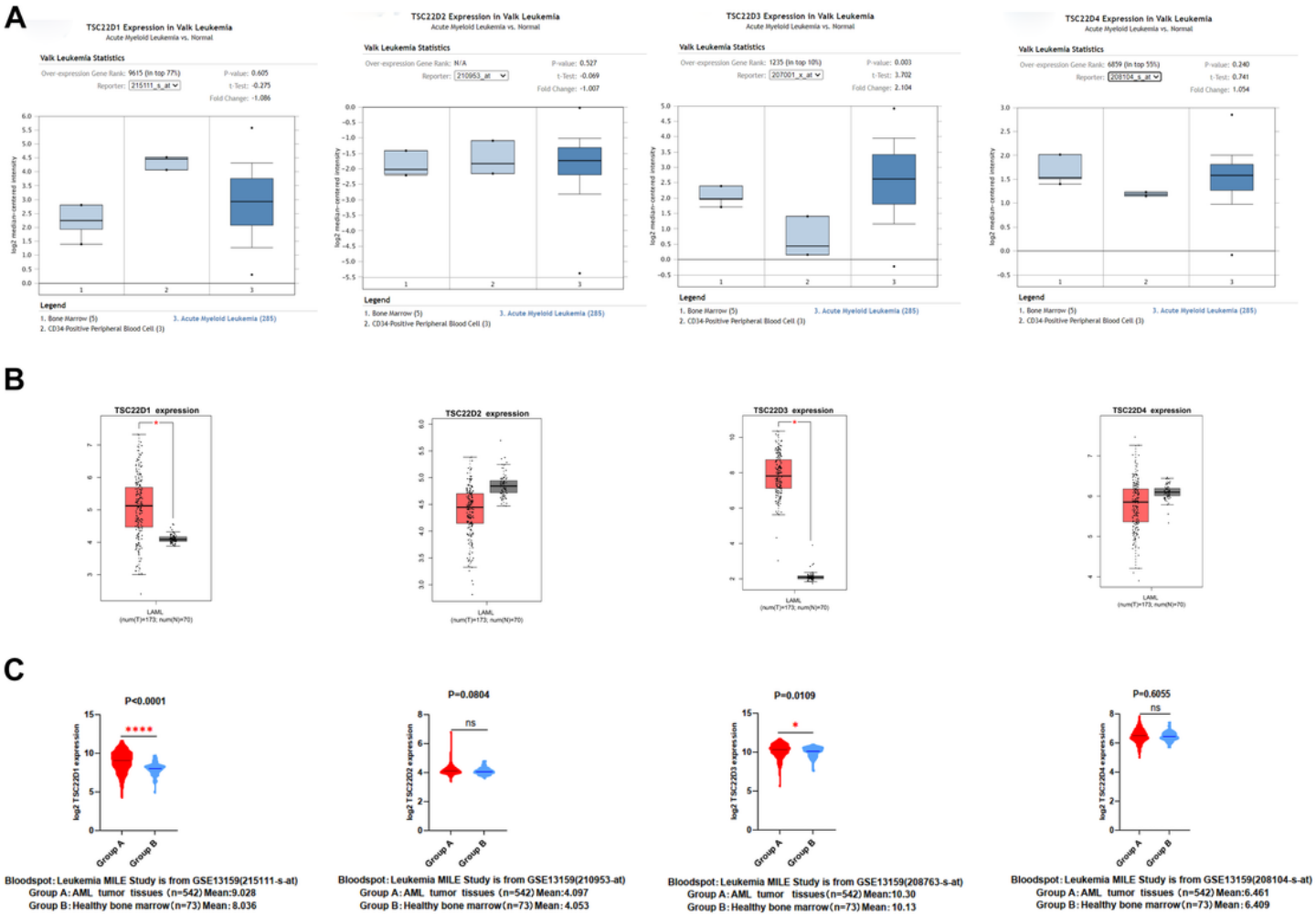

Figure 4. Genes expression analysis of the TSC22D domain family in AML group and normal control group. **(A)** The expression of the TSC22D domain family genes in healthy bone marrow and AML in the Valk leukemia dataset from the Oncomine database. **(B)** Boxplot displayed the expression of the TSC22D domain family genes in AML group and normal control group from TCGA in the GEPIA2 database. **(C)** Violin diagram showed the expression of the TSC22D domain family genes in healthy bone marrow group and AML group from GEO in the Leukemia MILE Study dataset from the Bloodspot database(*P<0.05, **P<0.01, ***P<0.001, ****P<0.0001,NS means no statistical significance).

Figure 4

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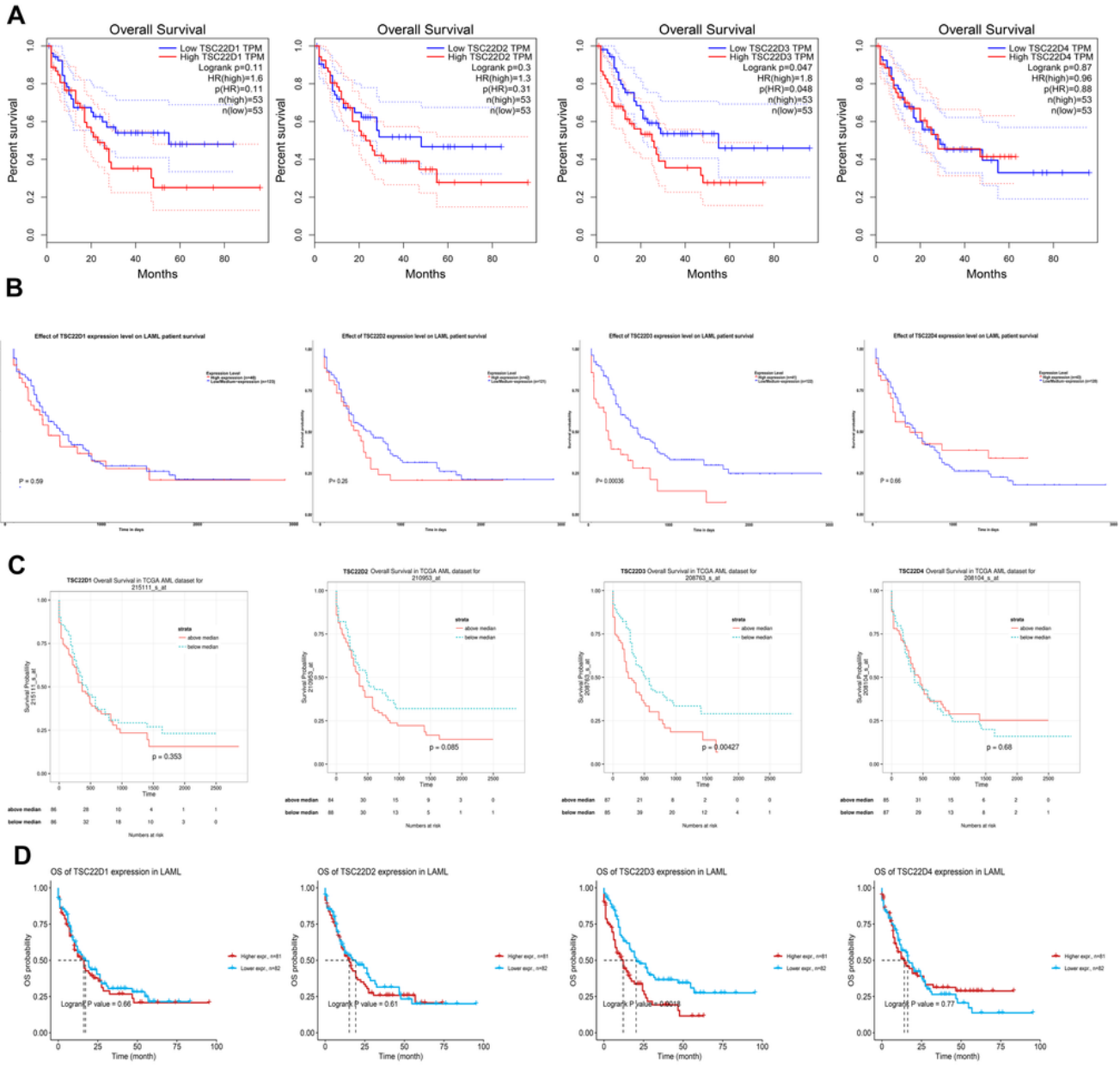

Figure 5. Overall survival(OS) of the TSC22D domain family genes in AML. **(A)** OS of 106 AML TCGA samples in the GEPIA2 database. **(B)** OS of 163 AML TCGA samples in the UALCAN database. **(C)** OS of 172 AML TCGA samples in the BloodSpot database. **(D)** OS of 163 AML TCGA samples in the GSCALite database.

Figure 5

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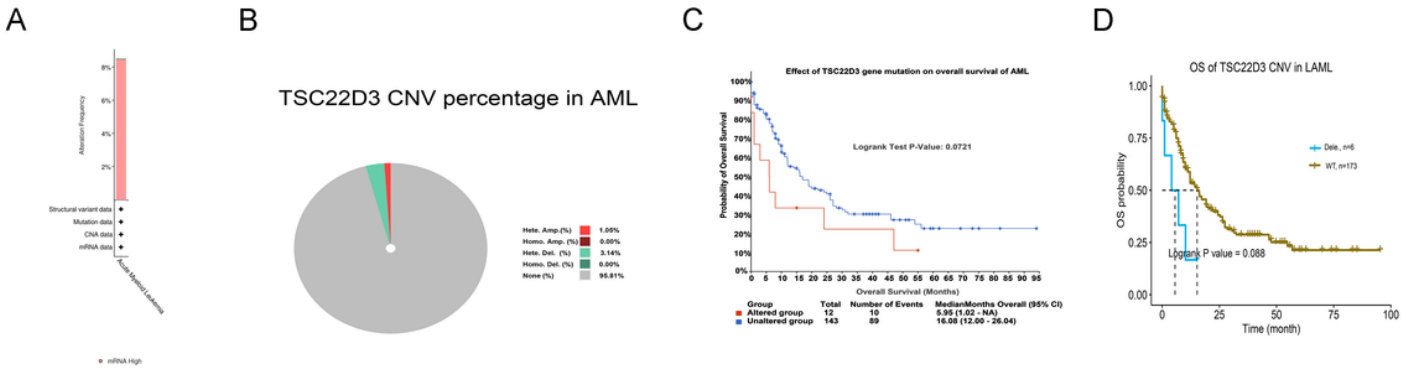

Figure 6. The profiles and OS of gene mutation and CNV of TSC22D3 in AML.**(A)** Gene mutation rate of TSC22D3 based on 165 AML samples from TCGA PanCancer Atlas in the cBioportal database. **(B)** CNV of TSC22D3 in AML in the GSCALite database.**(C)** Gene mutation of TSC22D3 impacted on OS of AML in the cBioportal database. **(D)** CNV of TSC22D3 impacted on OS of AML in the GSCALite database.

Figure 6

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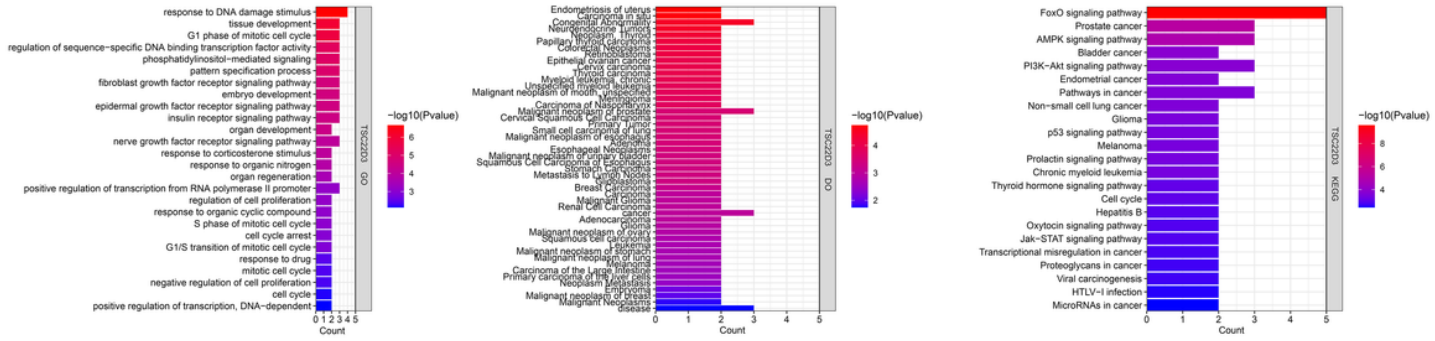

Figure 7. Functional enrichment analysis of TSC22D3. **(A)** Gene ontology biological process of TSC22D3 in the TRRUST database. **(B)** Diseases ontology of TSC22D3 in the TRRUST database.**(C)** KEGG pathway of TSC22D3 in the TRRUST database.

Figure 7

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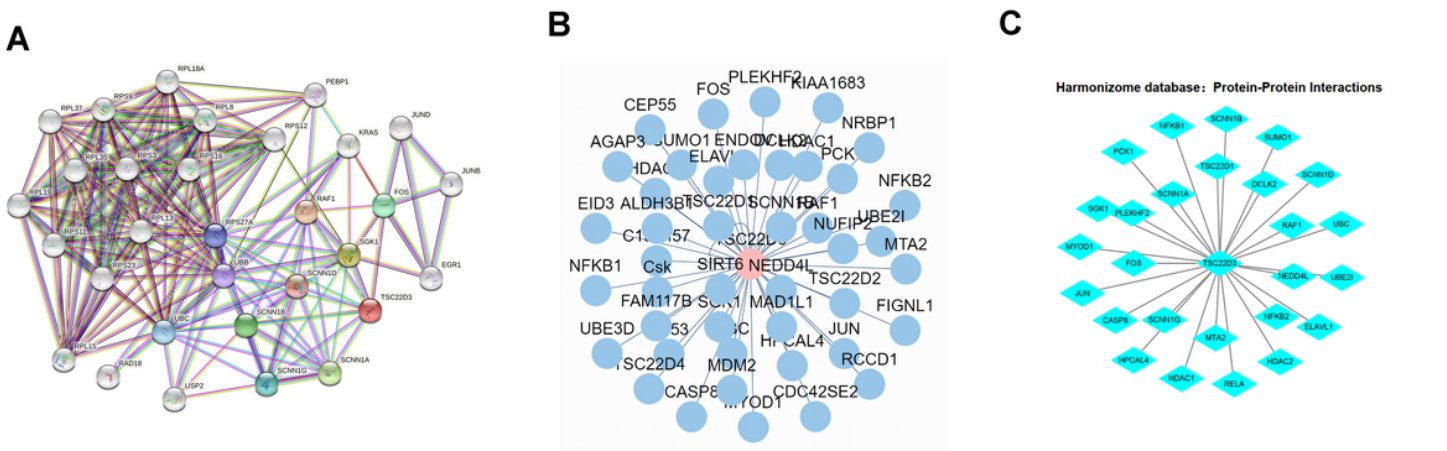

Figure 8. PPI analysis of TSC22D3.**(A)** PPI analysis of TSC22D3 in the String database. **(B)** PPI analysis of TSC22D3 in the AnimalTFDB3.0 database. **(C)** PPI analysis of TSC22D3 in the Harmonizome database.

Figure 8

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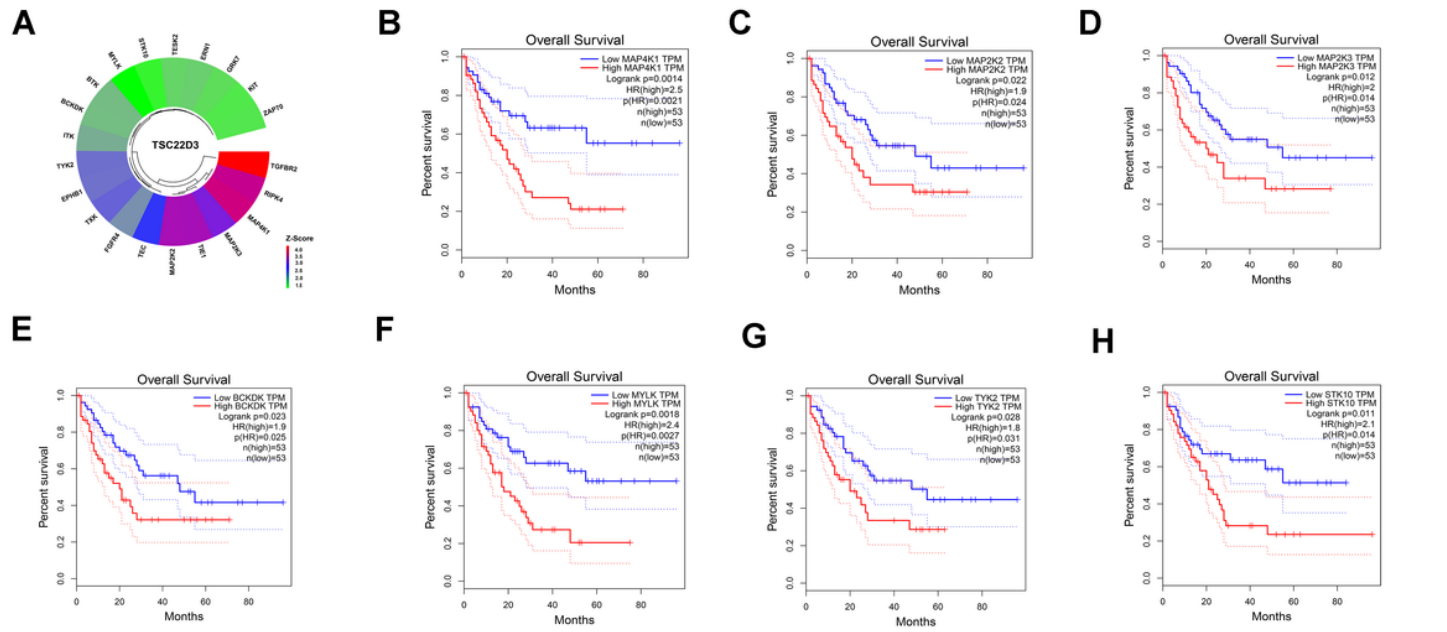

Figure 9. Analysis of TSC22D3 regulated kinases and effect on OS of AML.**(A)** Heatmap of the TOP20 TSC22D3 regulated kinases in the Harmonizome database.The color in the heatmap represented the level of z-score. **(B-H)** Effect of TSC22D3 regulated kinases on OS of AML in the GEPIA2 database.

Figure 9

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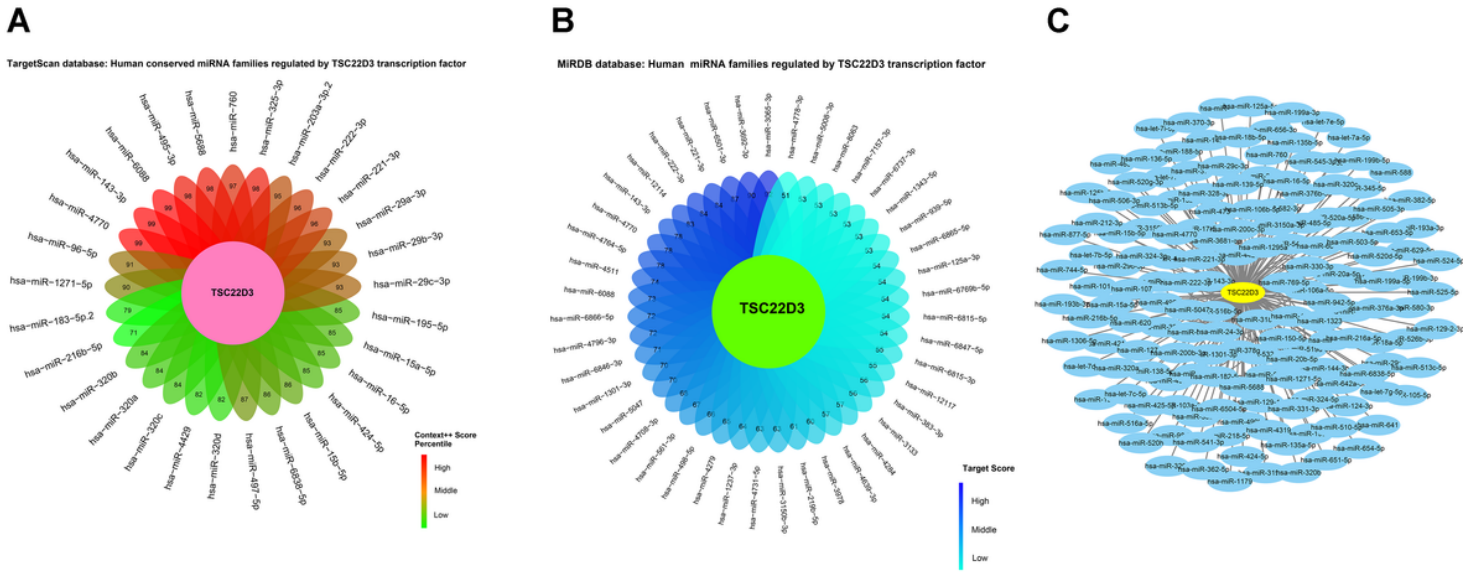

Figure 10. Analysis of regulated miRNAs of TSC22D3.**(A)** The flower plot of TSC22D3 regulated miRNAs in the TargetScan database.The red flower plot represented high context++ score percentile, the green flower plot represented low context++ score percentile.**(B)**The flower plot of TSC22D3 regulated miRNAs in the MiRDB database.The dark blue flower plot represented high target score, the wathet blue flower plot represented low target score.**(C)** The network diagram of TSC22D3 regulated miRNAs in the ENCORI database.

Figure 10

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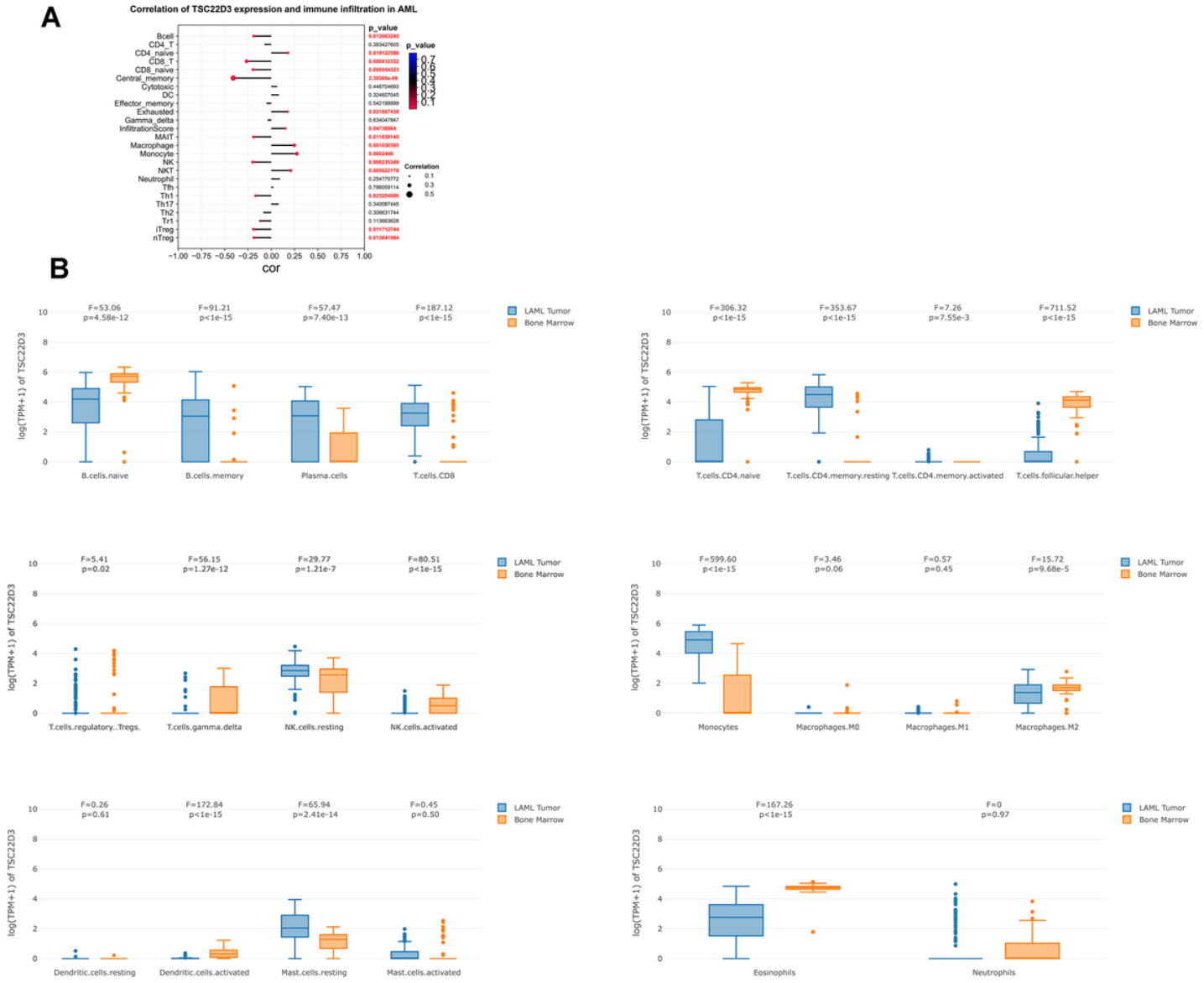

Figure 11. Immune Infiltration Analysis of TSC22D3 in AML. **(A)** Correlation of TSC22D3 expression and immune infiltration in AML in the GSCALite database. **(B)** CIBERSORT algorithm was used to analyze the relationship between TSC22D3 expression and immune infiltration in AML in the GEPIA2021 database.

Figure 11

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