

RESEARCH ARTICLE

OPEN ACCESS

ANALYSIS OF THE EXPRESSION PROFILE OF RPS19 IN SEPSIS AND A STUDY ON ITS VALUE FOR HIGH-PERFORMANCE DIAGNOSIS AND IMMUNOMODULATION

Qiu Yukai, Long Yan, Gu Xinbo, Zhang Ruonan, Zhu Haokai and Wang Qian

National Health Commission Key Laboratory of Control of Tropical Diseases, School of Life Sciences and Medical Technology, Hainan Medical University, Haikou, Hainan 571199, China

ARTICLE INFO

Article History:

Received 18th June, 2026
Received in revised form
19th July, 2026
Accepted 29th August, 2026
Published online 30th September, 2026

Key words:

Sepsis; Biomarker; RPS19;
Immunoregulation; WGCNA;
CIBERSORT.

*Corresponding author: Qiu Yukai

ABSTRACT

Sepsis is a life-threatening syndrome driven by infection-induced immune dysregulation. In this study, transcriptomic data (GSE243217) were analyzed by integrating DEG and WGCNA to screen sepsis-related core modules and hub genes. PPI network and ROC analyses were applied to identify key diagnostic genes, while CIBERSORT was used to evaluate immune infiltration and gene-immune correlations, with preliminary pharmacogenomic analysis performed. The MEbrown4 module ($\gamma = 0.85$) was strongly correlated with sepsis phenotypes, and RPS19 was recognized as the core hub gene. Functional enrichment indicated that RPS19 participates in immune response and protein synthesis. ROC analysis verified its perfect diagnostic efficiency (AUC = 1.0). Immune analysis showed that RPS19 expression was negatively correlated with pro-inflammatory M0 macrophages and $\gamma\delta$ T cells, implying its regulatory role in innate immunity during early sepsis. In addition, RPS19 may affect the sensitivity of sepsis patients to immunomodulatory drugs such as cisplatin. In conclusion, RPS19 serves as a promising diagnostic biomarker and immune regulator for sepsis, providing novel evidence for early molecular typing and targeted immune therapy.

Copyright©2026, Qiu Yukai et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Citation: Qiu Yukai, Long Yan, Gu Xinbo, Zhang Ruonan, Zhu Haokai and Wang Qian. 2026. "Analysis of the Expression Profile of RPS19 in Sepsis and a Study on Its Value for High-Performance Diagnosis and Immunomodulation". *International Journal of Development Research*, 16, (09), 70996-70999.

INTRODUCTION

Sepsis is a life-threatening disease caused by a dysregulated host immune response to infection, with exceedingly high morbidity and mortality (1). It is responsible for approximately 11 million deaths annually and remains one of the leading causes of mortality among patients in intensive care units (2–4). High-throughput transcriptomic technologies have provided powerful tools for elucidating the molecular mechanisms of sepsis. The integration of differential expression gene analysis with weighted gene co-expression network analysis enables effective identification of key driver modules and hub genes closely associated with disease clinical traits. Ribosomal protein S19 (RPS19), a component of the 40S ribosomal small subunit, has traditionally been linked to Diamond–Blackfan anemia through its gene mutations; however, recent studies have revealed its extra-ribosomal functions. In the inflammatory microenvironment, RPS19 dimers can serve as alternative ligands for complement factor C5a and, upon binding to C5a receptor 1 (C5aR1), exert antagonistic effects that inhibit monocyte recruitment and interfere with macrophage polarization. This mechanism has been preliminarily validated in pneumonia-induced acute lung

injury, suggesting that RPS19 may act as a critical bridge connecting protein synthesis and innate immune signal transduction. Furthermore, the dynamic evolution of immune cell infiltration is of equal importance during sepsis progression, and computational algorithms such as CIBERSORT enable the characterization of the immune microenvironment from transcriptomic data (5). Nevertheless, the precise role and diagnostic value of RPS19 in systemic inflammatory dysregulation of sepsis remain to be fully elucidated. In this study, based on the publicly available dataset GSE243217, we employ an integrated bioinformatics approach to systematically investigate the expression pattern, diagnostic performance, and immune infiltration correlation of RPS19 in sepsis, aiming to provide novel experimental evidence for early molecular subtyping and targeted immunomodulatory intervention in sepsis.

MATERIALS AND METHODS

Data Collection and Preprocessing: The sepsis transcriptomic dataset GSE243217 (6) was retrieved from the GEO database, comprising gene expression profiles from the

peripheral blood of 35 subjects (15 healthy controls and 20 sepsis patients). Raw data were log2-transformed and batch-effect-corrected using the sva and limma packages, and data quality and normalization were assessed via box plots.

Differential Gene Expression Analysis: Differential expression analysis was performed on the sepsis group and the healthy control group using the limma R package (7), with genes identified as differentially expressed if they met the threshold of $|\log_2FC| > 1$ and an FDR-corrected p-value < 0.05 .

Functional Enrichment Analysis: Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses were performed on co-expressed genes identified by the MEBrown4 module (8).

Protein-Protein Interaction (PPI) Network and Hub Gene Identification: Differentially expressed genes intersecting with the WGCNA module were input into the STRING database (v11.5, confidence score > 0.7) (9), and the PPI network was visualized and analyzed using the CytoHubba plugin in Cytoscape.

Evaluation of Diagnostic Performance and ROC Curve Modeling: ROC curve analysis was performed using the pROC package in R, and the AUC was used to quantify the sensitivity and specificity of each hub gene in distinguishing between sepsis patients and healthy individuals (10).

Immune Cell Infiltration Profile: We used the CIBERSORT deconvolution algorithm to infer the relative abundances of 22 immune cell subsets from RNA expression profiles (11), generating quantitative immune landscapes for each sample.

Exploratory Drug Sensitivity Analysis Based on Pharmacogenomics Databases: Using publicly available pharmacogenomic datasets from the GDSC1 and GDSC2 databases, we selected acute myeloid leukemia (LAML) and pancreatic adenocarcinoma (PAAD) models associated with immune activation and inflammation to analyze the Pearson correlation between RPS19 expression and cisplatin sensitivity.

RESULTS

Whole-Transcriptome Identification of Sepsis-Associated Modules and Key Genes: We performed integrated transcriptomic profiling on 35 peripheral blood samples from the GSE243217 dataset, comprising 15 healthy controls and 20 sepsis patients. Differential expression analysis was conducted using the limma package, with thresholds set at $|\log_2FC| > 1$ and adjusted $p < 0.05$, yielding a total of 3,756 DEGs between the sepsis and control groups. The volcano plot (Fig. 1A) revealed marked upregulation (yellow) and downregulation (blue) of multiple immune- and inflammation-related genes in the sepsis group, with significantly upregulated genes including S100A12, CLEC4D, and BCL2A1, whereas EIF4AY and others were substantially downregulated. The heatmap (Fig. 1B) further demonstrated a clear transcriptional separation between sepsis and control groups, supporting the robustness of DEG patterns in discriminating disease states.

In WGCNA, we selected a soft-thresholding power of 9 to ensure a scale-free network topology (scale-free $R^2 > 0.9$) with optimal mean connectivity. Multiple co-expression modules were identified and subsequently merged based on eigengene similarity (Fig. 1D). Correlation analysis between module eigengenes and clinical traits revealed that the MEBrown4 module exhibited the strongest positive correlation with the sepsis phenotype (correlation coefficient = 0.85, $p = 1 \times 10^{-10}$) (Fig. 1E).

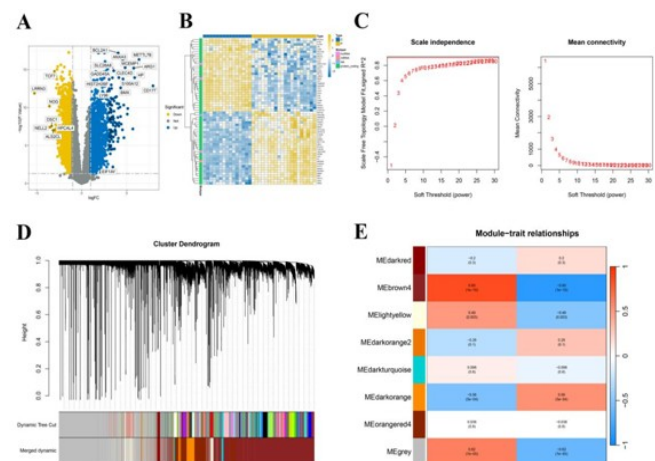


Fig. 1. Integrated transcriptomic analysis of sepsis-associated co-expression modules. (A) Heatmap of top DEGs between sepsis patients and healthy controls. **(B)** Volcano plot illustrating significantly upregulated (yellow), downregulated (blue), and non-significant (gray) genes. **(C)** Scale-free topology fitting indices and mean connectivity under different soft-thresholding powers for WGCNA. **(D)** Hierarchical clustering dendrogram of genes based on topological overlap. **(E)** Heatmap of module-trait correlations

Functional Enrichment and Network Analysis Reveal RPS19 as a Central Hub Gene in Sepsis: To prioritize disease associated genes, we intersected 3,756 differentially expressed genes (DEGs) with WGCNA derived co expression module genes and obtained 1,766 overlapping genes (Fig. 2A). GO and KEGG enrichment analyses of these overlapping genes revealed enrichment in immune regulation, ribosomal function and signal transduction. Major enriched terms included cytokine activity, RNA binding and cellular stress responses; enriched KEGG pathways comprised cytokine cytokine receptor interaction, MAPK and T cell receptor signaling, as well as COVID 19 related pathways, highlighting immune dysregulation as a key feature of sepsis (Fig. 2B, C).

PPI network analysis was performed using STRING and visualized in Cytoscape. Ribosomal proteins formed a tightly connected network, and RPS19, RPS18, RPS13, RPL5 and RPS5 were identified as top hub genes. RPS19 occupied the central position in the PPI network, implying its regulatory potential (Fig. 2D). ROC curve analysis was applied to assess the diagnostic performance of hub genes. RPS19 achieved an AUC of 1.000 for discriminating sepsis from healthy controls. Other hub genes also showed favorable diagnostic capacity: RPS18 (AUC = 0.877), RPS13 (AUC = 0.923), RPL5 (AUC = 0.957), RPS5 (AUC = 0.977) (Fig. 2E). A clinical nomogram incorporating these hub genes was further established to predict individual sepsis risk, in which RPS19 contributed markedly to total risk points (Fig. 2F).

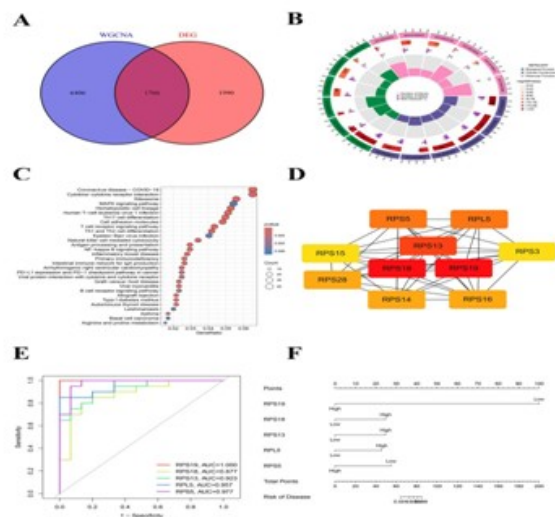


Fig. 2. Functional enrichment, and hub gene identification. (A) Venn diagram showing the overlap of DEGs and WGCNA module genes. **(B)** GO enrichment results. **(C)** KEGG pathway enrichment analysis. **(D)** Key hub genes. **(E)** ROC curves for five hub genes. **(F)** Nomogram model

Immune Cell Infiltration Profile Reveals the Immunoregulatory Role of RPS19 in Sepsis: The CIBERSORT algorithm was applied to estimate the relative abundances of 22 immune cell subpopulations based on bulk transcriptomic data. The heatmap (Fig. 3A) revealed marked differences in immune cell composition between the control and sepsis groups. Notably, the levels of neutrophils, monocytes, and macrophages M0 were significantly elevated in sepsis samples, whereas the proportions of CD8⁺T cells and resting memory CD4⁺T cells were markedly decreased. As shown in the violin plots, the fractions of multiple immune populations underwent significant changes in the sepsis group. Specifically, the proportions of neutrophils ($p < 0.001$) and monocytes ($p = 0.004$) were significantly increased, while CD8⁺T cells ($p = 0.007$) and Treg cells ($p = 0.001$) were substantially reduced (Fig. 3B). To further explore the immunomodulatory role of RPS19, Pearson correlation analysis was performed between RPS19 expression levels and the abundances of various immune cell types.

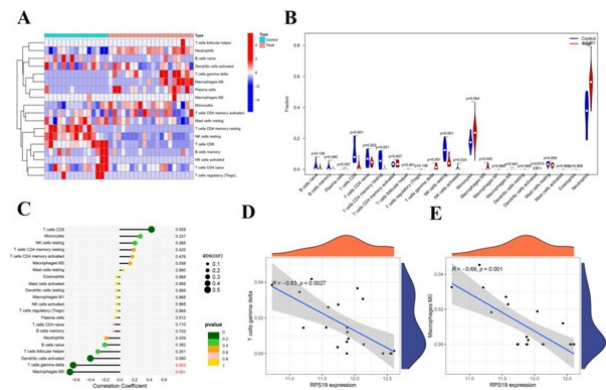


Fig. 3 RPS19 correlates with altered immune cell infiltration in sepsis. (A) Heatmap of CIBERSORT estimated relative abundances for 22 immune cell subsets in control and sepsis samples. **(B)** Violin plots comparing immune cell proportions between control (blue) and sepsis (red) groups; P values from Wilcoxon rank sum test. **(C)** Dot plot of Pearson correlations between RPS19 expression and immune cell infiltration; dot size denotes correlation magnitude, color denotes significance. **(D)** Negative correlation between RPS19 and γδ T cell abundance. **(E)** Negative correlation between RPS19 and M0 macrophage abundance.

The correlation dot plot demonstrated that RPS19 exhibited strong negative correlations with T cells gamma delta ($r = -0.63$, $p = 0.0027$) and macrophages M0 ($r = -0.68$, $p = 0.001$) (Fig. 3C). This relationship was further validated by scatter plots with marginal distributions, indicating that high RPS19 expression may be associated with the suppression of pro-inflammatory innate immune cell activity (Fig. 3D,E). **Exploratory Analysis of RPS19 Expression and Cisplatin Sensitivity:** To further investigate the potential role of RPS19 in drug response, we analyzed the association between RPS19 and cisplatin sensitivity in tumor cell lines using the GDSC1 and GDSC2 datasets. In the acute myeloid leukemia (LAML) model from GDSC1, RPS19 expression showed a moderate positive correlation with cisplatin sensitivity ($R = 0.36$, $p = 0.073$), suggesting that RPS19 expression may be associated with reduced cisplatin sensitivity. However, in the GDSC2-LAML model ($R = 0.17$, $p = 0.49$) and in the pancreatic adenocarcinoma (PAAD) model (GDSC1: $R = 0.028$, $p = 0.88$; GDSC2: $R = -0.14$, $p = 0.48$), the correlation between RPS19 and cisplatin sensitivity was weak or failed to reach statistical significance (Fig. 4).

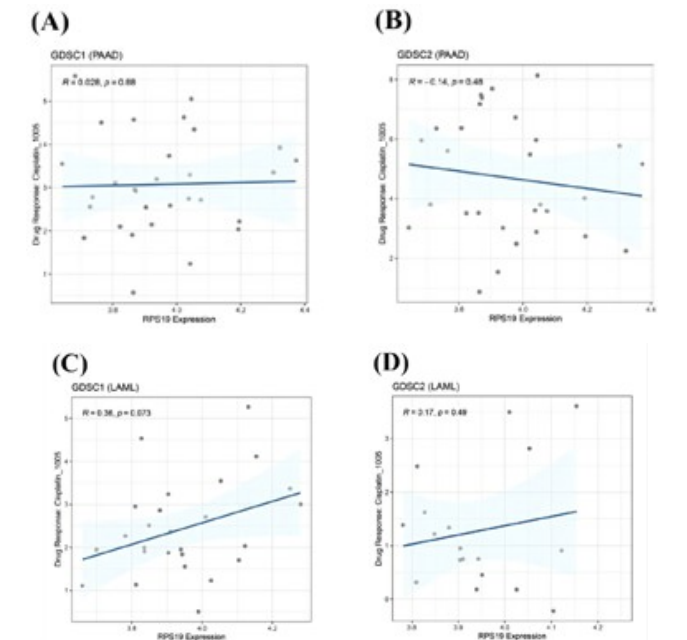


Fig. 4 Exploratory correlation between RPS19 expression and cisplatin response in cancer cell line models. (A) GDSC1-PAAD. **(B)** GDSC2-PAAD. **(C)** GDSC1-LAML. **(D)** GDSC2-LAML

CONCLUSION

Through comprehensive transcriptomic and immunoinformatic analyses, this study aimed to identify key genes associated with sepsis and identified RPS19 as a potential biomarker and immunomodulatory factor. Traditionally recognized as a ribosomal protein involved in protein synthesis (12), RPS19 has recently been increasingly implicated in immune regulation and inflammatory responses (13,14). By integrating differential gene expression analysis, WGCNA, immune cell deconvolution, and diagnostic performance evaluation, this study provides novel insights into the potential role of RPS19 in shaping the immune landscape of sepsis.

Funding: Provincial Undergraduate Training Program for Innovation and Entrepreneurship (No. S202611810018).

REFERENCES

- O'Brien Jr JM, Ali NA, Aberegg SK, *et al.* Sepsis (J). The American Journal of Medicine, 2007, 120(12), 1012–1022.
- Rudd KE, Johnson SC, Agesa KM, *et al.* Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study (J). The Lancet, 2020, 395(10219), 200–211.
- Prescott HC, Sussman JB, Wiersinga WJ. Postcritical illness vulnerability(J). Current Opinion in Critical Care, 2020, 26(5), 500–507.
- Rhee C, Dantes R, Epstein L, *et al.* Incidence and trends of sepsis in U.S. hospitals using clinical vs. claims data, 2009–2014 (J). JAMA, 2017, 318(13), 1241–1249.
- Chen B, Khodadoust MS, Liu CL, *et al.* Profiling tumor-infiltrating immune cells with CIBERSORT (J). Cancer Systems Biology: Methods and Protocols, 2018, 243–259.
- Muratsu A, Oda S, Onishi S, *et al.* Bacterial sepsis causes more dramatic pathogenetic changes in the Th1 pathway than does viral (COVID-19) sepsis: a prospective observational study of whole blood transcriptomes(J). Virology Journal, 2024, 21(1), 190.
- Ritchie ME, Phipson B, Wu DI, *et al.* limma powers differential expression analyses for RNA-sequencing and microarray studies(J). Nucleic Acids Research, 2015, 43(7), e47–e47.
- Yu G, Wang LG, Han Y, *et al.* clusterProfiler: an R package for comparing biological themes among gene clusters(J). Omics: A Journal of Integrative Biology, 2012, 16(5), 284–287.
- Szklarczyk D, Gable AL, Lyon D, *et al.* STRING v11: protein–protein association networks with increased coverage, supporting functional discovery in genome-wide experimental datasets(J). Nucleic Acids Research, 2019, 47(D1), D607–D613.
- Robin X, Turck N, Hainard A, *et al.* pROC: an open-source package for R and S+ to analyze and compare ROC curves(J). BMC Bioinformatics, 2011, 12, 1–8.
- Newman AM, Liu CL, Green MR, Gentles, *et al.* Robust enumeration of cell subsets from tissue expression profiles(J). Nature Methods, 2015, 12(5), 453–457.
- Draptchinskaia N, Gustavsson P, Andersson B, *et al.* The gene encoding ribosomal protein S19 is mutated in Diamond-Blackfan anemia(J). Nature Genetics, 1999, 21(2), 169–175.
- Nomura S, Ozaki Y, Ikeda Y. Function and role of microparticles in various clinical settings(J). Thrombosis Research, 2008, 123(1), 8–23.
- Yamamoto T. Molecular mechanism of monocyte-predominant infiltration in chronic inflammation: mediation by a novel monocyte chemotactic factor, the S19 ribosomal protein dimer(J). Pathology International, 2000, 50(11), 863–871.
