IECGE 2024 Conference

# The 2nd International Electronic Conference on Genes

11–13 December 2024 | Online

MDPI

# Identification of Biomarkers for Early Diagnosis and Prognosis in Sepsis: A Comprehensive Analysis

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## INTRODUCTION & AIM

Sepsis is a severe and life-threatening condition resulting from an excessive immune response to infection, leading to widespread inflammation, tissue damage, and multi-organ failure. In 2017, sepsis accounted for 19.7% of global fatalities, with India reporting one of the highest burdens, exceeding 4 million cases annually. Early detection and targeted interventions are critical for improving outcomes, yet current diagnostic methods lack sensitivity and specificity. MicroRNAs (miRNAs), small non-coding RNA molecules that regulate gene expression by binding to messenger RNAs (mRNAs) and inhibiting their translation or promoting their degradation, have emerged as promising biomarkers. Dysregulated miRNA expression plays a pivotal role in modulating the immune response during sepsis, making them potential tools for early diagnosis and prognosis. This study seeks to identify miRNAs involved in the dysregulated immune response during sepsis and evaluate their potential as predictive biomarkers. By uncovering key miRNAs, we aim to enhance diagnostic precision, guide therapeutic strategies, and deepen our understanding of sepsis progression, ultimately contributing to improved patient care and reduced global sepsis burden.

## METHOD

**Dataset collection and identification of DEGs and DEMs**

A)

| mRNA dataset | Control Vs Sepsis |
|---|---|
| GSE134364 (GPL17586) | 83 Control Vs 156 Sepsis |
| GSE236713 (GPL17077) | 30 Control Vs 125 Sepsis |
| GSE131761 (GPL13497) | 15 Control Vs 114 Sepsis |

B)

| miRNA dataset | Control Vs Sepsis |
|---|---|
| GSE94717 (GPL19449) | 3 Control Vs 12 Sepsis |
| GSE134358 (GPL21572) | 82 Control Vs 158 Sepsis |

**Table 1:** Gene Expression Omnibus (GEO) datasets A) mRNA datasets B) miRNA datasets

Data analysed by using GEO2R, P-value of 0.05, Log 2 FC (fold change) threshold >2

**Functional analysis and pathway enrichment analysis of DEGs**

The identified DEGs were analysed using ShinyGO, P-values < 0.05 and FDR < 0.05

**PPI network construction and identification of hub genes**

Cytoscape's MCODE (Molecular Complex Detection) plugin identifies highly linked proteins and key modules in STRING-analyzed networks (degree of interconnectedness >5) .

**Prediction and construction network of the miRNA-mRNA network**

The miRWalk database was used to identify the biological targets of differentially expressed miRNAs (DEMs) and identify those that overlapped with DEGs targets.

## RESULTS & DISCUSSION

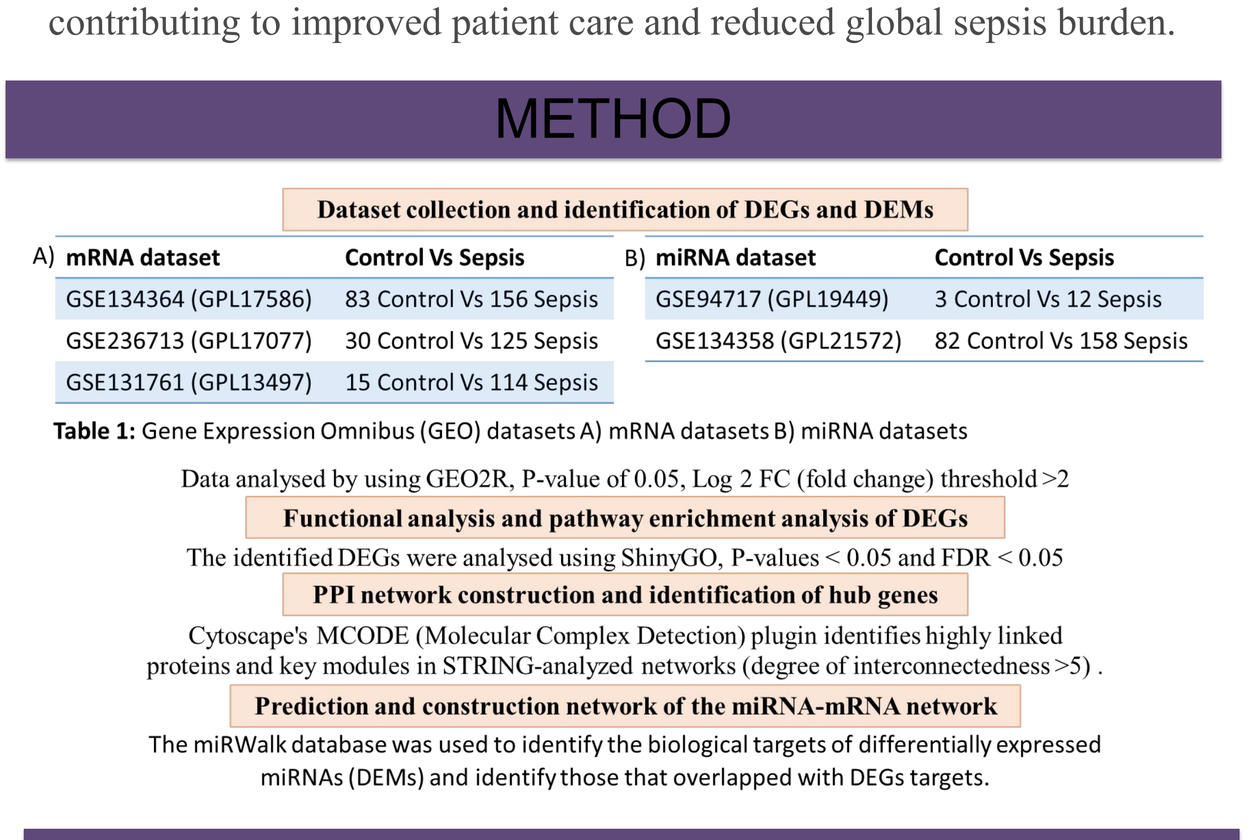


**Fig 1:** GO enrichment annotation and KEGG pathway analysis of the DEGs. A Top 20 BP (biological process) terms of DEGs. B Top 20 CC (cellular component) terms of DEGs. C Top 20 MF (Molecular Function) terms of DEGs. D Top 20 KEGG terms of DEGs using ShinyGo

## RESULTS & DISCUSSION

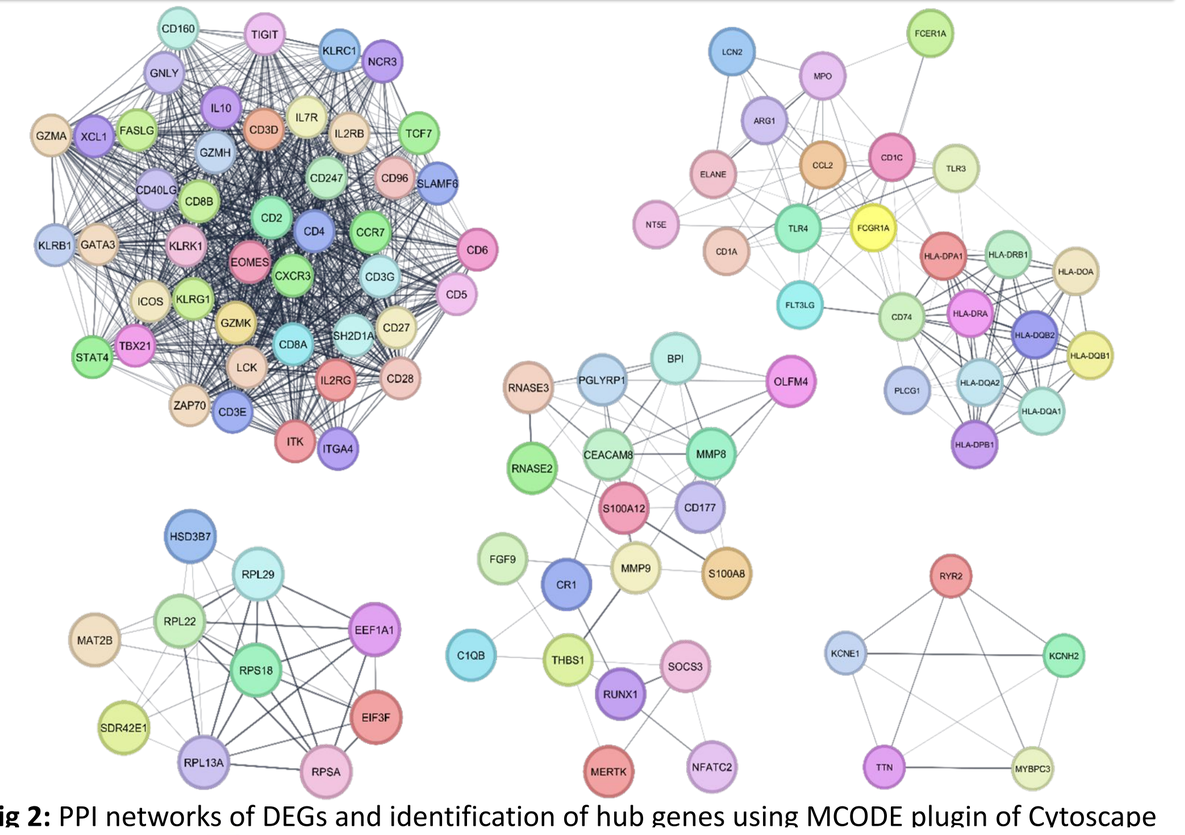


**Fig 2:** PPI networks of DEGs and identification of hub genes using MCODE plugin of Cytoscape

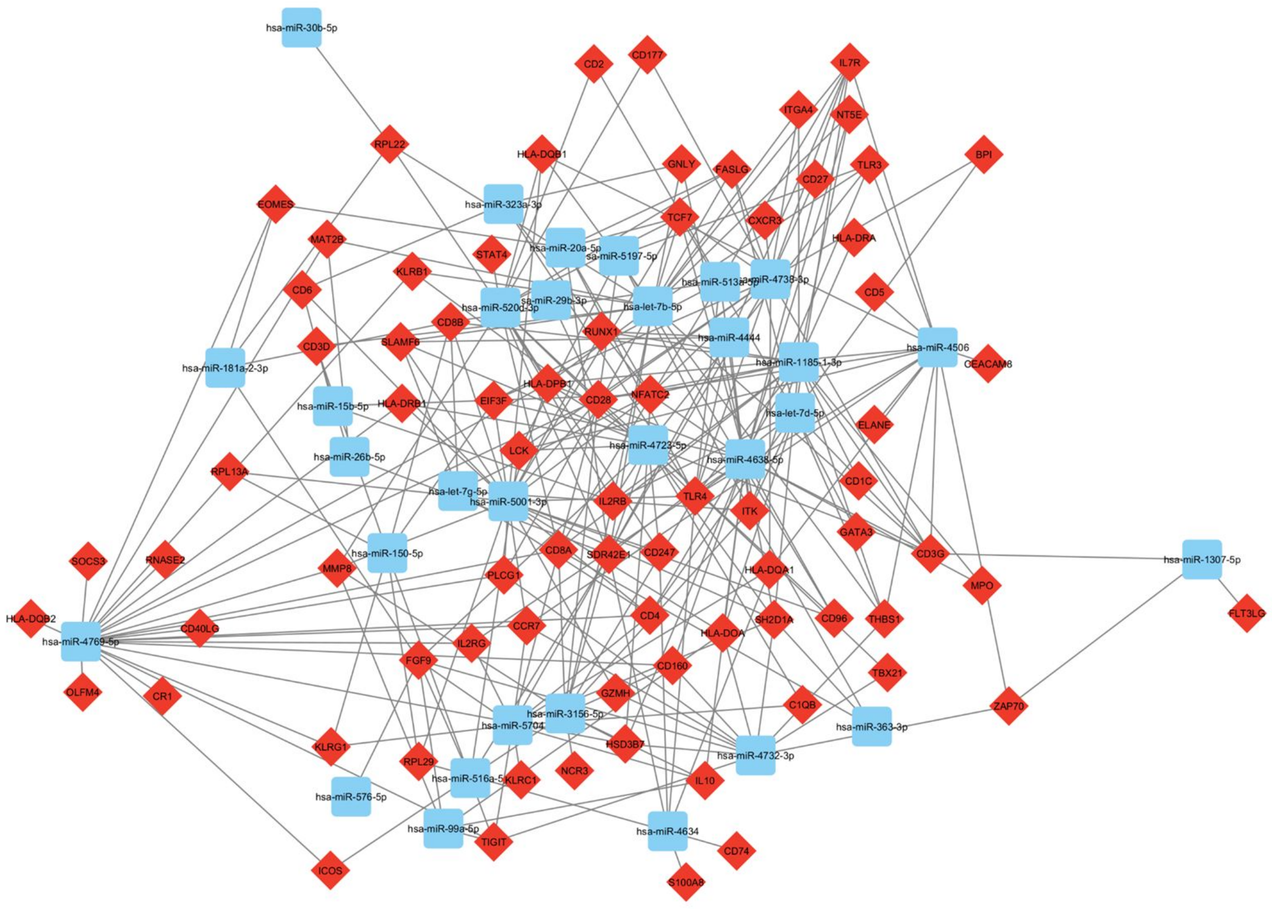


**Fig 3:** The miRNA-mRNA network of identified hub genes and DEMs using mirWalk and Cytoscape

## CONCLUSION

This study highlights miRNAs as key biomarkers for sepsis, with 837 DEGs and 98 hub genes identified. Upregulated SDR42E1, MAT2B, and CD28, and downregulated TLR4 and THBS1, interact with specific miRNAs (such as hsa-let-7d-5p, hsa-let-7b-5p, and hsa-miR-520d-3p), offering insights for the treatment. MMP8 showed an inhibitory effect, reducing excessive inflammation and tissue damage underscoring its therapeutic avenues.

## FUTURE WORK / REFERENCES

Future work should focus on developing miRNA-based therapies, such as miRNA mimics or inhibitors, and validating their efficacy in preclinical and clinical settings. This approach could revolutionize sepsis management, providing precision medicine tools to combat its devastating global impact.

**References:**

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2. Kong, C., Zhu, Y., Xie, X., Wu, J., & Qian, M. (2023). Six potential biomarkers in septic shock: a deep bioinformatics and prospective observational study. *Frontiers in immunology*, *14*, 1184700. https://doi.org/10.3389/fimmu.2023.1184700