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Type of Assignment : Individual Assignment
Tittle of Assignment : First Week's Assignment – Paper Summary (Transcriptomics)

Title
Transcriptomic analysis and laboratory experiments reveal potential critical genes and regulatory mechanisms in sepsis-associated acute kidney injury.

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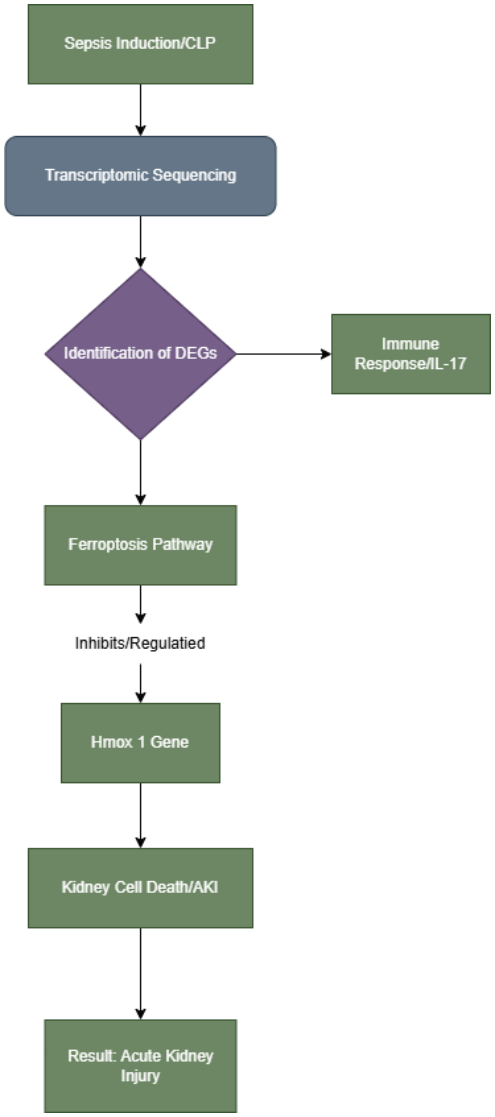
Introduction
Sepsis-associated acute kidney injury (SA-AKI) is a severe complication of sepsis, characterized by high morbidity and mortality in intensive care units. Despite its clinical prevalence, the complex pathophysiological mechanisms and transcriptional regulatory networks driving kidney damage in sepsis remain poorly understood. The objective of this research was to identify novel biomarkers, critical genes, and regulatory pathways involved in SA-AKI using a combination of high-throughput transcriptomic profiling and laboratory-based validation.

Methods
The researchers utilized a mouse model of sepsis induced by cecal ligation and puncture (CLP). Bulk messenger RNA (mRNA) sequencing was performed on kidney samples from CLP and control groups to identify differentially expressed genes (DEGs). Bioinformatics tools, including Gene Ontology (GO), KEGG, and Gene Set Enrichment Analysis (GSEA), were used to determine functional pathways. A protein-protein interaction (PPI) network was constructed to identify hub genes. Validation was conducted through quantitative real-time PCR (qPCR) and Western blotting. Additionally, the study explored the regulatory role of microRNAs (miRNAs), long noncoding RNAs (lncRNAs), and N6-adenosine methylation (m6A) regulators.



Results

The sequencing identified 4,754 DEGs. Pathway analysis revealed that these genes were significantly enriched in processes such as ferroptosis, apoptosis, and signaling pathways like PI3K-Akt, NF-kappa B, and IL-17. Notably, ferroptosis showed the highest enrichment score. Fifteen hub genes were identified, with seven (including Hmox1, Spp1, and Lcn2) showing significant involvement in the disease process. The researchers identified the mmu-miR-7212-5p-Hmox1 axis as a critical regulatory mechanism in ferroptosis during SA-AKI.

Discussion

The findings suggest that SA-AKI is not driven by a single pathway but by a complex network of cell death mechanisms and inflammatory responses. The identification of ferroptosis as a dominant pathway provides a new perspective on how renal cells are lost during sepsis. The study also highlights the epigenetic layer of regulation, showing that m6A RNA methylation regulators correlate closely with hub genes, suggesting that post-transcriptional modifications play a vital role in the progression of kidney injury.

Conclusion

The study successfully identified a comprehensive transcriptomic landscape of SA-AKI. The primary findings highlight the importance of the mmu-miR-7212-5p-Hmox1 axis and the role of ferroptosis in renal damage. These results provide potential therapeutic targets and biomarkers that could lead to more effective clinical interventions and a deeper understanding of the molecular pathogenesis of sepsis-induced kidney failure.

Bibliography

Wang, Z., Sun, R., Jiang, Z., Yang, K., Shao, Y., & Chen, X. (2022). Transcriptomic analysis and laboratory experiments reveal potential critical genes and regulatory mechanisms in sepsis-associated acute kidney injury. Scientific Reports, 12(1), 13615. https://doi.org/10.1038/s41598-022-17934-z