

REVIEWER'S REPORT

Manuscript No.: IJAR-58699

Title: Transcriptomic Horizons: The Emergence of RNA-Based Biomarkers for Prognostication After Cardiac Arrest,

Recommendation:

Accept as it is

Accept after minor revision.....

Accept after major revisionx.....

Do not accept (*Reasons below*)

Rating	Excel.	Good	Fair	Poor
Originality		x		
Techn. Quality			x	
Clarity			x	
Significance			x	

Reviewer's ID: JPR-142

Detailed Reviewer's Report

The manuscript provides a broad overview of mRNA, miRNA, lncRNA, circRNA and epitranscriptomic biomarkers and discusses sequencing technologies, bioinformatics, machine learning, multi-omics integration and challenges in clinical translation. The discussion of SLC2A1 and circulating miRNAs is particularly relevant.

However, several important issues should be addressed before publication. First, the manuscript does not adequately describe the literature-search and article-selection methodology. The authors should clarify whether this is intended as a narrative review or systematic review and provide an appropriate search strategy and selection rationale. Second, a comprehensive table summarizing the major transcriptomic biomarkers, sample type, sampling time, cohort size, neurological outcome, effect estimates/AUC, validation status and evidence level would substantially improve the manuscript.

Third, several quantitative and biomarker-specific claims require verification against the original studies. The reference list should be carefully audited because some citations do not appear to correspond adequately to the claims being made. For example, the section describing GSE200117 and hub-gene identification should be checked against its original source. In addition, the manuscript states that ten hub genes were identified but appears to list only nine genes, which should be verified and corrected.

Fourth, the manuscript should clearly distinguish discovery-stage biomarkers from independently validated biomarkers and should avoid implying that all discussed RNA candidates have equivalent clinical evidence. A stronger comparison with established neurological prognostic modalities and protein biomarkers such as NSE and NFL is also required.

Fifth, the sections dealing with epitranscriptomics and therapeutic targeting should be presented more cautiously because the clinical evidence remains preliminary. The limitations related to blood-cell

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composition, systemic inflammation, comorbidities, sampling time, longitudinal survivor bias and analytical standardization should be expanded.

Finally, the references require substantial formatting and completeness improvements. References currently described using "Science Direct" should be reformatted using the actual journal citation details. Language, grammar, spacing and terminology should also be carefully edited throughout the manuscript.

Overall, the manuscript is potentially valuable and addresses a timely subject, but substantial revision is required to improve scientific rigor, methodological transparency, citation accuracy and clinical interpretation.