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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 99897

Title: Extramural venous invasion in gastric cancer: 9.4T magnetic resonance imaging assessment and circular RNA functional analysis

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 08184535
Position: Peer Reviewer
Academic degree and professional title: Associate Professor
Reviewer's Country/Territory: Türkiye
Author's Country/Territory: China

Manuscript submission date: 2024-08-02

Reviewer chosen by: Jia-Lin Zhang

Reviewer accepted review: 2024-12-30 17:54

Reviewer performed review: 2025-01-01 06:07

Review time: 1 Day and 12 Hours

Scientific quality	Grade C (Good)
Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade B (Very Good)
Scientific significance of the conclusion in this manuscript	Grade B (Very Good)
Language quality	Grade B (Very good)
Does this manuscript describe a study of	Yes

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the existing knowledge system?	
Does this manuscript report a revolutionary innovation?	Yes
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Major revision
Re-review	No
Peer-reviewer statements	Peer-Review: Onymous
	Conflicts-of-Interest: No

SPECIFIC COMMENTS TO AUTHORS

Dear Author, Your submitted manuscript, "Extramural venous invasion mediated by hsa_circ_0097977 in orthotopic mouse model of gastric cancer," represents an important contribution to the field by investigating the role of extramural venous invasion (EMVI) and hsa_circ_0097977 in gastric cancer. The innovative use of MRI techniques and exploration of molecular mechanisms are among the notable strengths of your study. However, I would like to share some constructive suggestions to further enhance the clarity, impact, and readability of your work. Positive Feedback 1. Innovative Approach: The use of MRI for visualizing EMVI and investigating molecular mechanisms adds a novel dimension to the study. 2. Comprehensive Design: Integration of imaging, molecular, and histopathological analyses strengthens the research scope. 3. Significant Findings: The identification of hsa_circ_0097977's role in invasion and apoptosis of gastric cancer cells provides translational and clinical insights. Suggestions for Improvement 1. Title: • Assessment: The title is specific and reflects the core aspects of the study. However, it could be simplified to appeal to a broader audience. • Suggestion: Consider simplifying the title to: "The Role of hsa_circ_0097977 in Extramural Venous Invasion of Gastric Cancer." 2. Abstract: • Assessment: The abstract effectively

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summarizes the study's aims, methods, and findings but contains excessive technical details. • Suggestion: Focus on the main findings and implications, reducing the emphasis on technical procedures to improve readability. 3. Keywords: • Assessment: The keywords are appropriate but could include more variety. • Suggestion: Add terms like "circRNA," "mouse model," and "molecular imaging" to improve searchability. 4. Introduction: • Assessment: The introduction provides relevant background but is somewhat lengthy due to repeated references to the literature. • Suggestion: Present background information more concisely and emphasize the novel contributions of the study earlier in the section. 5. Methods: • Assessment: The methodology is thorough but includes an overwhelming level of detail that may detract from readability. • Suggestion: Consider including a flowchart summarizing the experimental design and providing more detailed explanations of animal ethics compliance. 6. Results: • Assessment: The results section is comprehensive but dense with technical data, making interpretation challenging. • Suggestion: Use summary tables to highlight key findings and simplify figure captions to make them more intuitive. 7. Discussion: • Assessment: The discussion relates findings to existing literature but lacks sufficient emphasis on clinical and translational implications. • Suggestion: Expand on the study's clinical significance and potential future applications, emphasizing how the findings could guide further research. 8. Figures and Tables: • Assessment: Figures and tables are relevant but lack consistency in format and clarity in descriptions. • Suggestion: Standardize formatting across all figures and tables and ensure that captions provide sufficient context. 9. Biostatistics: • Assessment: Statistical analyses are appropriate, but details about power analysis and sample size justification are missing. • Suggestion: Include information on power analysis and rationale for sample sizes to strengthen methodological transparency. 10. References: • Assessment: References are current and relevant but exhibit inconsistencies in formatting. • Suggestion: Ensure all references comply with

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the journal's required style and consider including additional recent studies for broader context. 11. Ethics Statement: • Assessment: Ethical approval is mentioned but briefly explained. • Suggestion: Elaborate on adherence to international standards for animal experiments to reassure readers of ethical compliance. Overall Evaluation Your manuscript makes a valuable contribution to the understanding of gastric cancer mechanisms. Implementing the suggested revisions would significantly enhance its scientific rigor, readability, and impact. In particular, refining the discussion to highlight clinical implications and simplifying methodological descriptions will help engage a broader readership. Thank you for your submission, and I hope these recommendations are helpful as you refine your work. Sincerely.

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Reviewer's code: 08399839
Position: Peer Reviewer
Academic degree and professional title: MD
Reviewer's Country/Territory: Türkiye
Author's Country/Territory: China

Manuscript submission date: 2024-08-02

Reviewer chosen by: Jia-Lin Zhang

Reviewer accepted review: 2025-01-01 16:32

Reviewer performed review: 2025-01-01 16:42

Review time: 1 Hour

Scientific quality	Grade B (Very good)
Novelty of this manuscript	Grade A (Excellent)
Creativity or innovation of this manuscript	Grade A (Excellent)
Scientific significance of the conclusion in this manuscript	Grade A (Excellent)
Language quality	Grade B (Very good)
Does this manuscript describe a study of	Yes

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the existing knowledge system?	
Does this manuscript report a revolutionary innovation?	Yes
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Minor revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Onymous
	Conflicts-of-Interest: No

SPECIFIC COMMENTS TO AUTHORS

Introduction: The introduction effectively sets the stage for the study; however, the transition from EMVI imaging findings to the molecular role of hsa_circ_0097977 could be made smoother. Suggestion: Clarify the rationale for selecting hsa_circ_0097977 among other circRNAs and how it specifically connects to EMVI. Methods: The methodology for constructing the orthotopic mouse model and performing MR imaging is detailed and well-described. Suggestion: Include more context on why a 9.4T MRI was chosen and whether this resolution is directly translatable to clinical imaging technologies. Suggestion: In the statistical analysis section, provide justification for the choice of Mann-Whitney U test in cell function assays. Results: The results are comprehensive, but some findings could benefit from clearer organization, particularly in the subsections discussing MR imaging and histopathological correlation. Suggestion: In "MR imaging-histopathological correlation analysis of EMVI in orthotropic models," clarify if there were any inter-observer discrepancies and how these were resolved. Suggestion: In the cell function test results, explicitly state if the apoptosis and proliferation results are consistent across all cell lines or if there are notable differences. Figures and Tables: Figures 4 and 5 are visually informative but could benefit from

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clearer annotations and arrows indicating key findings (e.g., tumor boundaries, EMVI features). Suggestion: Add short captions summarizing the clinical significance of each figure. Suggestion: Ensure that tables, particularly Table 2, clearly highlight statistically significant results (e.g., bold values or asterisk notations). Discussion: The discussion provides meaningful interpretations of the results; however, it could benefit from clearer comparisons to existing clinical literature. Suggestion: Expand on how hsa_circ_0097977 might act as a biomarker or therapeutic target in clinical settings. Suggestion: Discuss whether hsa_circ_0097977's modulation has potential implications for treatment strategies, such as targeted therapies or personalized medicine approaches. Clinical Relevance: While the study is preclinical, it would be valuable to elaborate on how findings could potentially guide clinical management of gastric cancer patients with EMVI. Suggestion: Provide hypothetical scenarios or clinical pathways where hsa_circ_0097977 detection and modulation could play a role in improving outcomes. Limitations: The limitations section addresses key constraints but could be expanded. Suggestion: Explicitly state that findings from preclinical models may not fully replicate human pathology. Suggestion: Highlight the small sample size and single-center design as factors limiting the generalizability of the results. Future Directions: Suggestion: Propose specific follow-up studies, such as larger animal studies, clinical trials, or bioinformatics analyses, to validate the role of hsa_circ_0097977. Suggestion: Discuss whether hsa_circ_0097977 could be integrated into existing diagnostic or prognostic models for gastric cancer. Language and Formatting: The manuscript is generally well-written, but minor grammatical inconsistencies are present. Suggestion: Conduct a thorough proofreading or consider professional language editing to improve clarity and readability. Overall Feedback: Your study is a significant contribution to the understanding of EMVI and its molecular regulation in gastric cancer. Addressing the above comments will strengthen the clarity, clinical relevance, and overall impact of the

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manuscript. Best regards, Dr. Mehmet Torun