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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 106564

Title: Pay attention to the value of liver regeneration in the re-compensation of decompensated cirrhosis

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 08384253

Position: Peer Reviewer

Academic degree and professional title: Associate Professor, MD, Professor

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2025-02-28

Reviewer chosen by: Shang Wu

Reviewer accepted review: 2025-03-12 13:55

Reviewer performed review: 2025-03-16 02:24

Review time: 3 Days and 12 Hours

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? Yes Is there any Key Word that is not included in the manuscript title? No Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes Are the Key Words complete? Yes
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Is the content of the Introduction adequate? **Yes**

Is the content of the Materials and Methods complete?
Yes

Is the description of the experiments clear and complete? **Yes**

Are the experimental data presented in the manuscript's biostatistics content reliable? **Yes**

Are the experimental data of the Results true and reliable? **Yes**

Are the quality and resolution of the images up to standard? **Yes**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **No**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Yes**

Is the content of the Discussion reasonable? **Yes**

Is the Conclusion reasonable? **Yes**

Are all references necessary and reasonable? **Yes**

Do authors omit important references? **No**

Are all references related to the topic of the manuscript? **Yes**

Do authors only cite their own earlier publications? **No**

Is the manuscript's text correct, concise, and clear? **Yes**

Will the manuscript's content be of interest to readers?
Yes

Are additional experiments needed for the study? **No**

Does the research scope comply with ethics? **Yes**



Scientific quality	Grade B (Very 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 A (Excellent)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Major revision
Re-review	No
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No

SPECIFIC COMMENTS TO AUTHORS

General Comments The manuscript provides a comprehensive review of the role of liver regeneration in recompensation for decompensated cirrhosis, emphasizing clinical implications and prognostic markers. While the topic is timely and aligns with emerging research on cirrhosis reversibility, several critical issues require attention to strengthen the scientific rigor, clarity, and novelty of the work. Below are specific comments organized by category: 1. Scientific Content and Originality Strengths: - The review synthesizes recent clinical evidence (e.g., Baveno VII criteria, HBV/HCV/alcohol-related recompensation studies) to challenge the traditional view of cirrhosis irreversibility. -



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Integration of liver regeneration markers (e.g., AFP, platelets) into prognostic models (e.g., BC2AID, TACIA scores) offers actionable insights for clinicians. Weaknesses: - Lack of Novelty: While the link between liver regeneration and recompensation is highlighted, the review largely reiterates existing knowledge without proposing novel mechanisms, therapeutic targets, or frameworks. For example, AFP's role as a regeneration marker is well-documented; deeper exploration of how AFP-driven regeneration structurally reverses fibrosis would enhance originality. - Limited Mechanistic Insights: The discussion of pathways (e.g., IL-6/STAT3 vs. IFN- γ /STAT1) is superficial. A detailed schematic summarizing molecular pathways driving regeneration in cirrhosis could improve clarity. - Overreliance on HBV Studies: Most cited data focus on HBV-related cirrhosis. Broader inclusion of other etiologies (e.g., MAFLD, autoimmune) would strengthen generalizability. 2. Methodology and Data Presentation Strengths: - Table 1 provides a structured overview of recompensation assessment dimensions. Weaknesses: - Incomplete Validation: The BC2AID and TACIA scores are mentioned but lack validation across diverse cohorts. Highlighting limitations (e.g., HBV-centric validation) is necessary. - Ambiguous Definitions: The Baveno VII criteria's liver function parameters (ALB, INR, bilirubin) lack standardized cut-offs. A comparative analysis of proposed thresholds (e.g., Wang et al. vs. Baveno VII) is needed. - Underdeveloped Table 1: The "Assessment methods" column is overly vague. For example, "precursor cell markers" should specify clinical assays (e.g., EpCAM/CK19 immunohistochemistry) and their feasibility. 3. Structure and Readability Strengths: - The manuscript is logically organized, with clear sections (e.g., liver regeneration mechanisms, recompensation criteria). Weaknesses: - Redundancy: Sections on AFP's prognostic value (e.g., paragraphs in "Role of Liver Regeneration") repeat similar points. Consolidate these into a focused subsection. - Overly Technical Language: Terms like "liver progenitor cells (LPCs)" and "STAT3 pathway" are introduced without sufficient context for



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non-specialists. A glossary or simplified explanations would aid readability. - Inconsistent Terminology: Use of "recompensation" vs. "re-compensation" should be standardized. 4. Future Directions and Clinical Relevance Strengths: - The call for individualized treatment strategies and regenerative capacity monitoring is clinically relevant. Weaknesses: - Unclear Research Gaps: Future directions (e.g., "further research on liver histopathology") are too generic. Specify actionable priorities (e.g., validating AFP in MAFLD cohorts, exploring IL-22 therapy). - Underdeveloped Clinical Applications: How can clinicians practically assess liver regeneration (e.g., AFP thresholds, imaging protocols)? Provide actionable recommendations. 5. Ethical and Technical Concerns - Referencing: The references are comprehensive but should be checked for proper formatting consistency. Some references have incorrect formatting of DOIs and PMID numbers. Additionally, some older references could be balanced with more recent studies to reflect the latest advancements in the field. 6. Language and Grammar - Minor Errors: - "recompensation" vs. "re-compensation" (standardize). - Awkward phrasing: "This also indicates that, in addition to the severity of liver injury, liver regeneration is a key determinant of liver failure prognosis." Recommendation Major Revision Required The manuscript addresses an important topic but requires substantial revisions to enhance originality, methodological clarity, and clinical applicability. Specific recommendations include: 1. Mechanistic Depth: Elaborate on molecular pathways (e.g., IL-6/STAT3) and their therapeutic implications. 2. Data Expansion: Include non-HBV etiologies and validate prognostic models in diverse cohorts. 3. Structural Refinement: Consolidate repetitive sections, simplify jargon, and standardize terminology. 4. Future Directions: Propose specific research priorities (e.g., regenerative biomarkers for MAFLD).



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Peer-review model: Single blind

Reviewer's code: 08246378

Position: Editorial Board

Academic degree and professional title: Associate Professor, MD, PhD

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2025-02-28

Reviewer chosen by: Hong-Xin Jiang

Reviewer accepted review: 2025-03-21 14:06

Reviewer performed review: 2025-03-24 08:21

Review time: 2 Days and 18 Hours

Content to be reviewed	Does the research scope comply with ethics? Yes Are additional experiments needed for the study? Yes Will the manuscript's content be of interest to readers? Yes Is the manuscript's text correct, concise, and clear? Yes Do authors only cite their own earlier publications? Yes Are all references related to the topic of the manuscript? Yes Do authors omit important references? Yes
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Are all references necessary and reasonable? **Yes**

Is the Conclusion reasonable? **Yes**

Is the content of the Discussion reasonable? **Yes**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Yes**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **Yes**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes**

Are the quality and resolution of the images up to standard? **Yes**

Are the experimental data of the Results true and reliable? **Yes**

Are the experimental data presented in the manuscript's biostatistics content reliable? **Yes**

Is the description of the experiments clear and complete? **Yes**

Is the content of the Materials and Methods complete? **Yes**

Is the content of the Introduction adequate? **Yes**

Are the Key Words complete? **Yes**

Does the Abstract contain the contents of each part of the manuscript (IMRaD)? **Yes**

Do authors' affiliations correspond to the content of the manuscript? **Yes**

Is there any Key Word that is not included in the manuscript title? **Yes**

Does the manuscript's content fall within the scope of the journal? **Yes**



Scientific quality	Grade B (Very good)
Novelty of this manuscript	Grade B (Very Good)
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 the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	Yes
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Major revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No

SPECIFIC COMMENTS TO AUTHORS

This paper focuses on the role of liver regeneration in the process of recompensation in patients with decompensated cirrhosis. The authors highlight that cirrhosis, characterized by diffuse liver fibrosis, typically progresses to decompensated stages with abnormal liver function and portal hypertension. Traditional beliefs have considered the transition from compensated to decompensated cirrhosis as irreversible. However, recent clinical evidence suggests that with effective treatment and management, some patients can experience reversal, leading to improved and stabilized liver function. The paper emphasizes liver regeneration as a crucial factor in this process, suggesting that



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restoring liver regeneration can promote recompensation and improve patient prognosis. Despite its importance, the role of liver regeneration in cirrhosis has received insufficient attention, prompting the authors to review its value. Comments and Suggestions for Improvement: 1. The abstract should be more concise and directly highlight the main findings and conclusions. Currently, it reads more like a background introduction rather than a summary of the paper's core content. 2. The introduction provides a good background on cirrhosis and its progression, but lacks recent references to support the changing perspective on reversibility. Incorporate recent high-impact studies to strengthen the argument. 3. The introduction could benefit from a clearer statement of the research gap and the paper's objectives. 4. Present results using tables, figures, and statistical significance levels to enhance readability and clarity. 5. The discussion section should delve deeper into the implications of the findings and how they contribute to the existing knowledge on liver regeneration and cirrhosis. 6. The conclusion should be more concise and directly summarize the main findings and their significance. 7. Use consistent terminology throughout the paper to avoid confusion. For example, clarify the distinction between "recompensation" and "liver regeneration." 8. Suggest updating the reference list to include recent and relevant publications that support the study's findings or provide additional context for the research. The following paper PMID: 39276679, 39185304 and 39081955 may be helpful. 9. Ensure that complex medical terms are defined or explained in simple language to enhance readability for a broader audience.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Manuscript NO: 106564

Title: Pay attention to the value of liver regeneration in the re-compensation of decompensated cirrhosis

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 08246378

Position: Editorial Board

Academic degree and professional title: Associate Professor, MD, PhD

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2025-02-28

Reviewer chosen by: Xin-Liang Qu

Reviewer accepted review: 2025-05-08 11:22

Reviewer performed review: 2025-05-08 11:54

Review time: 1 Hour

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? Yes Is there any Key Word that is not included in the manuscript title? Yes Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes Are the Key Words complete? Yes
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Is the content of the Introduction adequate? **Yes**
Is the content of the Materials and Methods complete?
Yes
Is the description of the experiments clear and
complete? **Yes**
Are the experimental data presented in the
manuscript's biostatistics content reliable? **Yes**
Are the experimental data of the Results true and
reliable? **Yes**
Are the quality and resolution of the images up to
standard? **Yes**
Do the selection and design of the figures and tables
follow the principles of necessity and clarity? **Yes**
Is there any duplication between various parts of the
manuscript and between the main text and the content
presented in the figures and tables? **Yes**
Are the figures and tables numbered consecutively in
the order in which they appear in the manuscript? **Yes**
Is the content of the Discussion reasonable? **Yes**
Is the Conclusion reasonable? **Yes**
Are all references necessary and reasonable? **Yes**
Do authors omit important references? **Yes**
Are all references related to the topic of the
manuscript? **Yes**
Do authors only cite their own earlier publications? **Yes**
Is the manuscript's text correct, concise, and clear? **Yes**
Will the manuscript's content be of interest to readers?
Yes
Are additional experiments needed for the study? **Yes**
Does the research scope comply with ethics? **Yes**



Scientific quality	Grade A (Excellent)
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 A (Excellent)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	Yes
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Accept
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No

SPECIFIC COMMENTS TO AUTHORS

I am pleased with the additional work done in response to my comments and I recommend this manuscript for publication.