



**Baishideng  
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**https://www.wjgnet.com**

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 112566

**Title:** Hydrogen peroxide pathway in ulcerative colitis: Promises and challenges in translating novel pathogenesis to clinical practice

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 08758352

**Position:** Peer Reviewer

**Academic degree and professional title:** Assistant Professor, PhD

**Reviewer's Country/Territory:** India

**Author's Country/Territory:** China

**Manuscript submission date:** 2025-07-30

**Reviewer chosen by:** Hong-Xin Jiang

**Reviewer accepted review:** 2025-08-25 04:48

**Reviewer performed review:** 2025-08-25 05:19

**Review time:** 1 Hour

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

Is the content of the Materials and Methods complete?  
**Not Applicable**

Is the description of the experiments clear and complete? **No**

Are the experimental data presented in the manuscript's biostatistics content reliable? **No**

Are the experimental data of the Results true and reliable? **No**

Are the quality and resolution of the images up to standard? **Not Applicable**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Not Applicable**

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? **Not Applicable**

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

Is the Conclusion reasonable? **Yes**

Are all references necessary and reasonable? **No**

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? <b>Yes</b> Does the research scope comply with ethics? <b>Not Applicable</b>
Scientific quality	Grade C (Good)
Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade C (Good)
Scientific significance of the conclusion in this manuscript	Grade C (Good)
Language quality	Grade D (Fair)
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	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

### SPECIFIC COMMENTS TO AUTHORS

The manuscript presents a thoughtful commentary on Dr. Pravda's review regarding hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) as a pathogenic driver in ulcerative colitis (UC). The authors highlight both the promise of this novel hypothesis and the challenges in translating it into clinical practice. The topic is timely and relevant, with potential implications for



therapeutic innovation. However, there are areas that require refinement for clarity, rigor, and completeness.

1. The commentary effectively contextualizes Pravda's hypothesis within broader UC research but should emphasize more clearly what new insights this letter adds beyond summarizing limitations of the original review. Strengthening the authors' own critical perspective would enhance the contribution.
2. The manuscript rightly calls for randomized controlled trials (RCTs), but it would be valuable to suggest specific trial designs (e.g., patient subgroups, endpoints, comparator arms). This would make the recommendations more actionable.
3. The commentary is well-organized but could improve transitions between sections (e.g., from "Clinical Evidence" to "Reconciling with Contemporary Understanding"). Currently, it reads as a series of critiques rather than a cohesive argument.
4. The authors raise concerns about long-term safety of reducing agents but provide little detail. This section would benefit from citing toxicology data, known adverse effects, or knowledge gaps requiring systematic study.
5. While the manuscript critiques selective evidence synthesis in Pravda's review, it occasionally falls into similar selectivity by citing limited recent studies. Including a broader range of references (e.g., large-scale genetic and microbiome studies) would give the commentary more authority.
6. If novel reducing agents are to be tested, ethical concerns (first-in-human trials, compassionate use, risk-benefit justification) should be discussed. This would show awareness of practical hurdles beyond just clinical trial design.
7. The manuscript lacks visual elements. A summary table comparing:  
H<sub>2</sub>O<sub>2</sub> hypothesis vs. other UC mechanisms .  
Proposed therapies vs. current standard of care would help readers quickly grasp the argument.



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8. Ensure all abbreviations (UC, IBD, RCT, ROS, JAK) are defined at first use in the main text.



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**Title:** Hydrogen peroxide pathway in ulcerative colitis: Promises and challenges in translating novel pathogenesis to clinical practice

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 08005849

**Position:** Peer Reviewer

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

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** China

**Manuscript submission date:** 2025-07-30

**Reviewer chosen by:** Hong-Xin Jiang

**Reviewer accepted review:** 2025-08-13 00:27

**Reviewer performed review:** 2025-09-08 03:01

**Review time:** 26 Days and 2 Hours

<b>Content to be reviewed</b>	Does the manuscript's content fall within the scope of the journal? <b>Yes</b> Is there any Key Word that is not included in the manuscript title? <b>Yes</b> Do authors' affiliations correspond to the content of the manuscript? <b>Yes</b> Is the content of the Introduction adequate? <b>Not Applicable</b> Is the content of the Materials and Methods complete?
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## Not Applicable

Is the description of the experiments clear and complete? **Not Applicable**

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

Are the Key Words complete? **Yes**

Are the experimental data presented in the manuscript's biostatistics content reliable? **Not Applicable**

Are the experimental data of the Results true and reliable? **Not Applicable**

Are the quality and resolution of the images up to standard? **Not Applicable**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Not Applicable**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **Not Applicable**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Not Applicable**

Is the content of the Discussion reasonable? **Not Applicable**

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**



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	Is the manuscript's text correct, concise, and clear? <b>Yes</b> Will the manuscript's content be of interest to readers? <b>Yes</b> Are additional experiments needed for the study? <b>No</b> Does the research scope comply with ethics? <b>Not Applicable</b>
Scientific quality	Grade B (Very good)
Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade C (Good)
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?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Accept
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

## SPECIFIC COMMENTS TO AUTHORS

I agree with Wang's perspective. While acknowledging the possibility of the hypothesis presented in Pravda's paper, the authors highlight biases in the cited literature, weak



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evidence, and omissions in previous studies. I believe these are scientifically fair and reasonable arguments. Pravda's hypothesis should be recognized as one argument. Still, the point linking the use of immunosuppressants to the interests of pharmaceutical companies seems more like a political argument than a scientific one. If widely shared with the public, it could lead patients to discontinue or refuse to use medication. Wang et al.'s claims explain the background behind the current treatment and serve as a warning against rushing to adopt new treatment methods. Furthermore, they summarize the current issues and present future research directions. Based on the above points, this paper is worthy of publication.



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 112566

**Title:** Hydrogen peroxide pathway in ulcerative colitis: Promises and challenges in translating novel pathogenesis to clinical practice

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 08005849

**Position:** Peer Reviewer

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

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** China

**Manuscript submission date:** 2025-07-30

**Reviewer chosen by:** Cong Lin

**Reviewer accepted review:** 2025-09-26 13:09

**Reviewer performed review:** 2025-09-26 19:43

**Review time:** 6 Hours

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

Is the content of the Materials and Methods complete? **Not Applicable**

Is the description of the experiments clear and complete? **Not Applicable**

Are the experimental data presented in the manuscript's biostatistics content reliable? **Not Applicable**

Are the experimental data of the Results true and reliable? **Not Applicable**

Are the quality and resolution of the images up to standard? **Not Applicable**

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? **Not Applicable**

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?



	<b>Yes</b> Are additional experiments needed for the study? <b>No</b> Does the research scope comply with ethics? <b>Yes</b>
<b>Scientific quality</b>	Grade A (Excellent)
<b>Novelty of this manuscript</b>	Grade B (Very Good)
<b>Creativity or innovation of this manuscript</b>	Grade B (Very Good)
<b>Scientific significance of the conclusion in this manuscript</b>	Grade A (Excellent)
<b>Language quality</b>	Grade B (Very good)
<b>Does this manuscript describe a study of the existing knowledge system?</b>	Yes
<b>Does this manuscript report a revolutionary innovation?</b>	No
<b>Does this manuscript report an unconventional innovation?</b>	Yes
<b>Conclusion</b>	Accept
<b>Peer-reviewer statements</b>	Peer-Review: Anonymous
	Conflicts-of-Interest: No
<b>Are your review comments generated by AI tools?</b>	No

### **SPECIFIC COMMENTS TO AUTHORS**

The authors have revised the manuscript in accordance with the comments provided in the peer review report, adequately addressing all questions. I believe that the scientific quality, language quality, and ethical documentation of the revised manuscript meet the publication standards. I appreciate the authors' enthusiasm and expertise. --- The authors have revised the manuscript in accordance with the comments provided in the



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peer review report, adequately addressing all questions. I believe that the scientific quality, language quality, and ethical documentation of the revised manuscript meet the publication standards. I appreciate the authors' enthusiasm and expertise. --- The authors have revised the manuscript in accordance with the comments provided in the peer review report, adequately addressing all questions. I believe that the scientific quality, language quality, and ethical documentation of the revised manuscript meet the publication standards. I appreciate the authors' enthusiasm and expertise. --- The authors have revised the manuscript in accordance with the comments provided in the peer review report, adequately addressing all questions. I believe that the scientific quality, language quality, and ethical documentation of the revised manuscript meet the publication standards. I appreciate the authors' enthusiasm and expertise. --- The authors have revised the manuscript in accordance with the comments provided in the peer review report, adequately addressing all questions. I believe that the scientific quality, language quality, and ethical documentation of the revised manuscript meet the publication standards. I appreciate the authors' enthusiasm and expertise. --- The authors have revised the manuscript in accordance with the comments provided in the peer review report, adequately addressing all questions. I believe that the scientific quality, language quality, and ethical documentation of the revised manuscript meet the publication standards. I appreciate the authors' enthusiasm and expertise. --- The authors have revised the manuscript in accordance with the comments provided in the peer review report, adequately addressing all questions. I believe that the scientific quality, language quality, and ethical documentation of the revised manuscript meet the publication standards. I appreciate the authors' enthusiasm and expertise. --- The authors have revised the manuscript in accordance with the comments provided in the peer review report, adequately addressing all questions. I believe that the scientific quality, language quality, and ethical documentation of the revised manuscript meet the publication standards. I appreciate the authors' enthusiasm and expertise. ---