

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 75384

Title: Evidence-based pathogenesis and treatment of ulcerative colitis: A causal role for colonic epithelial hydrogen peroxide

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04010086

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2022-01-25

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-26 07:13

Reviewer performed review: 2022-02-04 09:50

Review time: 9 Days and 2 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No
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SPECIFIC COMMENTS TO AUTHORS

This is an extraordinarily interesting manuscript for the pathogenesis mechanism and treatment of ulcerative colitis. The author put the theory that it is hydrogen peroxide in the colonic epithelial cells but not immune regulation is crucial in the process of ulcerative colitis. This hypothesis does have scientific significance and the author proves the hypothesis in the manuscript well in some aspects. However, this manuscript needs some revision before publication. In this manuscript, the author cited a great number of references. Overall, the abstract can represent the content of this manuscript. The keywords precisely summarized this study. The introduction demonstrated the background of this research, illustrated what is controversial to date, and induced a scientific question. This part supported the content of the manuscript well. A significant limitation of this manuscript is this manuscript was not organized and presented as the structure of evidence-based medicine should be. For the title, the scientific hypothesis of this article is the enrichment of hydrogen peroxide in the colonic epithelial cells drives inflammatory bowel disease and the intervention of pathological hydrogen peroxide signaling can lead to long-term relief of ulcerative colitis. I think the title does not reflect this hypothesis comprehensively and thoroughly. In the abstract, the conclusion of "Cumulative data indicate that individuals with ulcerative colitis have normal immune systems and current treatment guidelines calling for modification of the immune response based on the belief that ulcerative colitis is caused by an underlying immune dysfunction is not supported by the evidence and potentially very harmful" might be too radical; because some studies have indicated the immune factors played a role in the pathogenesis process of ulcerative colitis, and there might not sufficient

evidence of the harmfulness of immune therapy to ulcerative colitis patients. Other problems are listed below. 1. As is mentioned above, the organization of this manuscript is more likely a review instead of an evidence-based medicine study. In each part the author explained the background, including some possible hypotheses, and proved it via references, making it probably a structure of a literature review. 2. The author does cite numerous references, but there might be a lack of literature screening and evidence level determination process. 3. If the author wants to publish this manuscript as an evidence-based medicine study but without PRISMA 2009 Checklist, it might be imperative to explain the reason. 4. Some of the subtitles are intriguing but cannot summarize the subsequent content, such as 1.1 and 4.6 5. Part 5 mentioned “evidence-based” treatment, but in the result part (5.3), only one patient was reported. Basically, it might be imperative to provide the demographic data and the inclusion/exclusion criteria of these patients. If the author wants to convince the readers the study design is indeed evidence-based, I think the author should add the method part to illuminate the study design. And some statistical description might be also needed. In conclusion, this manuscript might be more likely publishing as a review instead of an evidence-based study under the author’s current work and some revisions.

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Peer-review model: Single blind

Reviewer's code: 00503545

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Director, Doctor

Reviewer's Country/Territory: Japan

Author's Country/Territory: United States

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Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-28 08:11

Reviewer performed review: 2022-02-05 12:25

Review time: 8 Days and 4 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No
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SPECIFIC COMMENTS TO AUTHORS

In this paper, the author presents experimental and clinical evidence that identifies hydrogen peroxide produced by the colonic epithelium as the causal agent in the pathogenesis of ulcerative colitis. This paper is well written and the content of the paper is clinically interesting. However, the author should address the following points. 1. I think that this paper is too long as an article in the academic journal. I suggest that the paper is shorten. 2. With regard to "Evidence based treatment", I suggest that this theme is submitted as an independent paper.