

PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

Manuscript NO: 58317

Title: The Clinical Relevance of Intestinal Barrier Dysfunction in Gastrointestinal Diseases

Reviewer's code: 03967085

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Bulgaria

Author's Country/Territory: Germany

Manuscript submission date: 2020-07-21

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2020-09-07 20:25

Reviewer performed review: 2020-09-07 20:52

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input 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 Grade E: Do not publish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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The title is informative and relevant. The references are relevant and recent. The cited sources are referenced correctly. Appropriate and key studies are included. The introduction reveals what is already known about this topic. the data are discussed from different angles and placed into context without being overinterpreted. The conclusions answer the aim of the study. The conclusions are supported by references and own results. This study added to what is already in the topic. The article is consistent within itself. Specific comments on weaknesses of the article and what could be improved: The role of stem cell therapy for the improvement of barrier function

RESPONSE TO REVIEWER 1

- **Comment from Reviewer 1:** Reviewer 1 noted that the role of stem cell therapy for the improvement of barrier function could improve the manuscript

Author Response: Thank you for your suggestion regarding the role of stem cell therapy to improve barrier function. *In vivo* transplant of epithelial organoids or pluripotent stem cells into the intestinal tract to support epithelial growth/barrier function is a promising therapeutic approach to treat gastrointestinal pathology. While we agree the role of stem cell therapy has relevance in the context of gastrointestinal diseases and would be an interesting topic to explore, the scope of our manuscript does not include a review of emerging therapies or therapeutic targets. Therefore, it does not appear that reviewing of the role of stem cell therapy to improve barrier function is consistent with the scope of the manuscript's aims. We made not edits to the manuscript based on this comment.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

Manuscript NO: 58317

Title: The Clinical Relevance of Intestinal Barrier Dysfunction in Gastrointestinal Diseases

Reviewer's code: 00034489

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Germany

Manuscript submission date: 2020-07-21

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2020-09-04 12:37

Reviewer performed review: 2020-09-11 01:22

Review time: 6 Days and 12 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="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors aim to review for intestinal barrier on gastrointestinal disease. The review is professionally written. However, the reviewed diseases are restricted to IBD, IBS, and immune checkpoint inhibitor colitis. The unhandled many diseases such as intestinal infection, NSAIDs induced enteropathy, coeliac disease, etc. produce injury to intestinal barrier. The title should be changed to clear the contents of the review.

RESPONSE TO REVIEWER 2

- **Comment from Reviewer 2:** Reviewer 2 noted that the scope of the review is restricted to IBD, IBS, and immune checkpoint inhibitor colitis and does not cover all gastrointestinal diseases such that the title should be changed.

Author Response: Thank you for your suggestion regarding relationship between the title of the manuscript and gastrointestinal disease covered in the review. We agree with the reviewer that the manuscript does not exhaustively review all gastrointestinal diseases (e.g. NSAID-induced enteropathy, coeliac disease). We also agree with the reviewer that the title should be changed to reflect the contents of the review. Therefore, we changed the title of the manuscript to “The Clinical Relevance of Intestinal Barrier Dysfunction in Common Gastrointestinal Diseases.” We also reviewed and revised the content of the manuscript as to not imply that the contents of the review cover all gastrointestinal diseases. Our rationale for including the term “common” in the title of the manuscript is because irritable bowel syndrome (IBS) and irritable bowel disease, both covered in the review, are common gastrointestinal diseases. The prevalence of IBS is approximately 11%;¹ Crohn’s disease (CD) and ulcerative colitis (UC) have a prevalence of approximately 200 per 100,000 adults in North America.² The

manuscript also covers an emerging pharmacotherapy-associated gastrointestinal disorder: immune checkpoint inhibitor-associated colitis. This class of drugs continues to grow in the number of approved indications and use in clinical practice. For example, a cross-sectional study found that the estimated number of cancer patients eligible for checkpoint inhibitor therapy increased from 1.54% in 2011 to 43.64% in 2018.³ Thus, checkpoint inhibitor-associated colitis is expected to become more common over time.

1. Canavan C, West J, Card T. The epidemiology of irritable bowel syndrome. *Clin Epidemiol.* 2014;6:71-80. Published 2014 Feb 4. doi:10.2147/CLEP.S40245.
2. Kappelman MD, Rifas-Shiman SL, Kleinman K, et al. The prevalence and geographic distribution of Crohn's disease and ulcerative colitis in the United States. *Clin Gastroenterol Hepatol.* 2007;5(12):1424-1429. doi:10.1016/j.cgh.2007.07.012.
3. Haslam A, Prasad V. Estimation of the Percentage of US Patients With Cancer Who Are Eligible for and Respond to Checkpoint Inhibitor Immunotherapy Drugs. *JAMA Netw Open.* 2019;2(5):e192535. Published 2019 May 3. doi:10.1001/jamanetworkopen.2019.2535.