

PEER-REVIEW REPORT

Name of journal: *World Journal of Meta-Analysis*

Manuscript NO: 66881

Title: Preclinical safety, effectiveness evaluation, and functional bacterial screening of fecal microbiota transplantation based on germ-free animals

Reviewer's code: 02537773

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Academic Research, Associate Professor, Doctor, Lecturer

Reviewer's Country/Territory: Germany

Author's Country/Territory: China

Manuscript submission date: 2021-04-08

Reviewer chosen by: Ze-Mao Gong

Reviewer accepted review: 2021-07-29 15:33

Reviewer performed review: 2021-07-29 21:28

Review time: 5 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input checked="" type="checkbox"/> Grade E: Do not publish
Language quality	<input 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 checked="" 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



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SPECIFIC COMMENTS TO AUTHORS

The review by Yang et al. aims to review the advantage of germ-free animals as a tool to improve the safety, effectiveness in FMT. The idea is novel, but fails to meet the clinical expectations. Unfortunately, I may need to disagree on multiple aspects of introduction including safety, standardization. Several international guidelines are available that provide highly standardized protocols on FMT in *C. difficile* (by the way it call *Clostridioides difficile*). The experience of the past years clearly shows that with appropriate indication FMT has no issues with acceptability. If performed at high (minimal) quality standards FMT is a safe method. Therefore the great question is if germ free mice would provide any benefit in this regard in particular for CDI. Going through the review, I was not convinced by the scientific discussion and rationale. There are multiple limitations related to xenograft microbiota studies.

PEER-REVIEW REPORT

Name of journal: *World Journal of Meta-Analysis*

Manuscript NO: 66881

Title: Preclinical safety, effectiveness evaluation, and functional bacterial screening of fecal microbiota transplantation based on germ-free animals

Reviewer's code: 05610189

Position: Peer Reviewer

Academic degree: MD

Professional title: Research Fellow

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2021-04-08

Reviewer chosen by: Ze-Mao Gong

Reviewer accepted review: 2021-07-28 08:29

Reviewer performed review: 2021-08-10 10:17

Review time: 13 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" 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 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



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SPECIFIC COMMENTS TO AUTHORS

Dear Editor-in-chief, The manuscript I had the pleasure to review by Ya-Peng Yang is a review article on the open issues regarding fecal microbiota transplantation. The Authors give a general overview on the available evidence about safety, standardization and effectiveness evaluation of FMT. Moreover, in this review, the Authors propose a new model based on germ-free mice to assess the safety and the effectiveness of FMT. The content of the paper is certainly of interest and the language is generally good; however, it is quite hard to understand the aim of the manuscript. It seems that the authors want to give a clear review of the state-of-art but, at the same time, wants to give a very personal interpretation of the matter. Furthermore, it isn't clear whether Authors did use the presented model or just propose it. Since the structure of the manuscript is quite confounding to the reader, I would recommend clarifying its aim and structure. If the Authors want to propose a new animal model for FMT assessment I would recommend modifying the chosen article type (e.g. Field of Vision, Opinion Review, Letter to the Editor). Moreover, I would recommend providing experimental data about the use of the proposed model by the Authors themselves or by other research groups. On the other side, if the Authors prefer focusing on a review article, I would recommend some modifications:

- Authors should present how they performed the review of the literature.
- The paper should strongly benefit from a summarizing table about presented articles.
- I would suggest rephrasing the subtitles. It would be preferable that Authors' personal comments, which are certainly very valuable, should be at the end of the dissertation and not the main topic of the review; otherwise, it would become a 'viewpoint' rather than a 'narrative review'.
- I would also suggest expanding the comment about safety since this represents the major ethical issue to consider in future for very needed randomized studies (e.g. PMID: 29592876, 32574415, ...).

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Reviewer's code: 05610189

Position: Peer Reviewer

Academic degree: MD

Professional title: Research Fellow

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2021-04-08

Reviewer chosen by: Man Liu

Reviewer accepted review: 2021-10-18 15:40

Reviewer performed review: 2021-10-20 10:18

Review time: 1 Day and 18 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 type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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SPECIFIC COMMENTS TO AUTHORS



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Dear Editor in Chief, the Authors have addressed all the raised issues. The paper now provides a complete Authors' viewpoint. I believe the publication as an "Opinion Review" is more appropriate.