

PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

Manuscript NO: 61372

Title: The microbiota, renal disease and renal transplantation

Reviewer's code: 05232520

Position: Peer Reviewer

Academic degree: BSc, MSc, PhD

Professional title: Professor, Research Scientist

Reviewer's Country/Territory: Brazil

Author's Country/Territory: Italy

Manuscript submission date: 2020-12-04

Reviewer chosen by: Li Ma

Reviewer accepted review: 2020-12-04 19:59

Reviewer performed review: 2020-12-10 19:26

Review time: 5 Days and 23 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 Grade E: Do not publish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
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

SPECIFIC COMMENTS TO AUTHORS

The manuscript submitted by Salvadori and Tsalouchos, aims to review the role of intestinal microbiota in renal diseases and renal transplantation. Despite the importance of this subject to the area, the manuscript presents outdated concepts, need a more concise and organized presentation of the ideas, and lacks criticism. Below, I have addressed my major and minor concerns Major concerns: • In “Definitions”, authors stated that “More than 100 trillion bacteria live in our body, which represents more than 10 times the number of cells in our body”. However, it is of common knowledge that 10:1 is not the right proportion. This assumption refers to data published back in the 1970’s, which were reviewed some years ago. Thus, it will be of paramount importance if authors update this information. To clarify this, please read the article below: 1. Sender R, Fuchs S, Milo R. Revised Estimates for the Number of Human and Bacteria Cells in the Body. PLoS Biol. 2016 Aug 19;14(8):e1002533. doi:10.1371/journal.pbio.1002533.PMID:27541692; PMCID:PMC4991899. • Metabolites are of one the best ways to describe how gut microbiota is able to interact or modulate the physiology of different organs and systems. Thus, it is mandatory to improve this discussion, deeply exploring the role of gut bacteria-derived metabolites in health and disease. In addition, the text lacks a more comprehensive description of the interactions between gut microbiota, nervous, immunological and endocrine system, which together, have a great impact on disease outcome, including renal disease, and organ transplantation. • Cytokines are not only diffused throughout the body because of gut barrier dysfunction, this assumption needs to be rewritten and improved. • In general, the references listed in text are outdated and need to be reviewed e.g. The number of Th cells arising from or associated with gut microbiota goes far beyond Th1, Th2 and Th17 cells. Also, it is of common knowledge that some bacteria, such as segmented filamentous bacteria, induce the physiologic differentiation of Th17 cells, however, the

review describes that such differentiation only occurs in a dysbiotic environment. Thus, authors need to clarify and improve these assumptions. • Authors need to explore in text the terms: indigenous microbiota, pathobionts and pathogens. Further, it is crucial to use proper terms rather than good and bad bacteria. It is known that depending on the context the same bacteria may play a beneficial or detrimental role. • The text needs to be better structured. In its current form it is quite confusing to understand the role and the relationship of bacteria, immune system and their interaction with other organs or biological systems. Also, several aspects concerning gut microbiota composition, roles (locally and systemically), metabolites, and aspects dictating the description of “healthy microbiota”, need to be broadly and thoroughly explored. It will be better if authors started by depicting gut microbiota, its composition, aspects dictating eubiosis and dysbiosis, besides the role of metabolites influencing local and distant organs and systems, including, but not exclusively, immune system and kidneys physiology. Afterwards, authors must narrow this subject to establish a critical and concise relationship with kidney diseases, renal transplantation and immunosuppressive therapies. • It is mandatory to segregate animal from human studies. Indeed, such categorization will improve the knowledge about the “state of the art” concerning experimental and clinical studies. • As the review is focused on the role of gut microbiota on renal transplantation and diseases, the section “Therapy for gut dysbiosis” must be renamed to something more appropriate. E.g. Microbial therapies in kidney health, disease and transplantation. • The term microbiota has been wrongly used throughout the text. Microbiota, refers to all microorganisms inhabiting some specific niche (gut, skin, lungs, etc). Microbiota encompasses bacteria, viruses, fungi and archaea. Despite their major contribution in this scenario, it is wrong to use the term microbiota as a synonym of bacteria and vice-versa. • Authors must include a section with future perspectives in the manuscript

Minor concerns: • The text has some typos e.g.

interleukine (correct form: interleukin).

PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

Manuscript NO: 61372

Title: The microbiota, renal disease and renal transplantation

Reviewer's code: 03766962

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Reviewer's Country/Territory: China

Author's Country/Territory: Italy

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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

1. You can detail the relation between renal relative diseases and microbiota in the part of introduction, and cite some references to support what you want to elaborate. Second, The typesetting of the article needs to be greatly revised, each paragraph is too short, and the theoretical support is insufficient. Third, the main idea in the part of abstract is not clear. Fourth, the function of microbiota can be described more detail and more comprehensive, I can not learn the "frontier" knowledge from your article. Finally, the figure you can make it looks more professionally. So, I think your article need to major revision.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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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
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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

I have no further comments.