

Dear Reviewers,

Thank you for your very insightful feedback. I have revised the article and my responses are described below.

**Reviewer's code:** 05817597

Authors reviewed the relationship between gut microbiome dysbiosis and solid organ transplantation (liver, kidney, lung, heart, gut). Gut microbiomes regulates pro-inflammatory cytokines, induces tolerance, and regulates immune cells through metabolites such as butyrate, acetate and propionate. Use of antibiotics and immunosuppressants in transplant settings would alter gut microbiome (blooms of pathobionts, loss of commensals and loss of diversity) and increase risks of rejection, also influences pharmacokinetics of immunosuppressants. Challenges in rigorous microbiome studies and establishing causal relationships had been pointed out by authors in discussion part. The manuscript is in general informative but requires modifications as follows: 1. The keywords and core tips parts were shown in the manuscript information but not included in the manuscript file. 2. The methodology was not well described for this review (e.g. What search engine was used with what keywords? How many literatures had been reviewed and review period? English-only literatures or not? etc.) It is suggested to have a table illustrating the relationship between gut microbiome dysbiosis and effects of different types of solid organ transplantation (liver, kidney, lung, heart, gut) separately. Many of the references are related to kidney and liver transplants while those addressing other solid organ transplants (lung, heart, gut) are lacking. 3. The strengths and limitations of this review had not been addressed. 4. Please ensure correct formatting for references (e.g. ref 40 and 41) and proper alignment and line spacing for the text.

- 1. The keywords and core tips parts were added.*
- 2. The methodology was added as a separate paragraph*
- 3. Limitations of studies have been addressed*

*4. Formatting for references (e.g. ref 40 and 41) corrected and proper alignment and line spacing for the text.*

**Reviewer's code:** 05821735

1 y 2.The title and the abstract is adequate with the topic ,raises the hypothesis and the studies that speak on the subject. 3.The article does not contain the keywords. I think it is important to add them. 4. The review is significant considering that it is a new topic and there is still much to be investigated 5. The research is a complete review, does not require statistical analysis, but clearly mentions relevant articles on the subject. 6.The article makes an extensive review that includes all relevant aspects in solid organ transplantation. Mentioning preclinical and clinical studies. 7.It allows to know quickly the advances in the subject and encourages to study and investigate more on the subject. 8. Does'nt apply 9 y 10By the type of revision does not require statistical analysis or use of SI units 11.Taking into account the novelty of the subject, he makes a very extensive bibliographic search that supports the revision very well. The manuscript cite adequately the important and autorative references. 12.The manuscript is properly written and drafted. The review of the subject is presented in an order that allows visualizing the importance of continuing to investigate due to the current clinical relevance. 13. I am not sure about the author prepare the manuscript according to the appropriate research methods. 14. Doesn't apply In general, I consider the manuscript to be a good quality revision. Its importance lies in raising the relevance of the topic in organ transplantation The research explore the nascent field of gut microbiome.While evidence supporting the importance of the gut microbiome in the health of HSCT patients has been accumulating, it is unclear if these findings will also be applicable to SOT recipients.

*Added keywords.*

**Reviewer's code:** 05821400

It is an interesting topic to review and lot has been done in past. This review mainly covers the pathophysiology with very little clinical implication. In my opinion following

areas should be addressed separately to link it to the clinical aspect of transplantation: 1. Rejection 2. GI flora and bioavailability of immunosuppressants 3. Role of fecal transplant. It will also be good to add some flowcharts and tables to improve the visual impact of the paper.

*1. Included a study linking dysbiosis to rejection. Also discussed mouse models linking gut flora to rejection.*

*2. Section on immunosuppressants and gut flora deals with pharmacokinetics and bioavailability of immunosuppressants.*

*3. I didn't include fecal transplant as it has mainly been studied in the context of C. diff infection and studies in solid organ transplant recipients without C. diff are lacking.*

Thank you,

Aparna Sharma