

#### Reviewer 1 (05821532)

Sayuri Yoshikawa et al reported a review: Advantageous tactics with certain probiotics for the treatment of graft-versus-host-disease after hematopoietic stem cell transplantation, it is clinically appealing. **Thank you very much for the good evaluation on our manuscript.**

I agreed that this review is considered for publication, but some errors should be corrected.

1. Authors should re-polish the paper with many grammar and syntax errors, especially article use **According to this suggestion, again we have gone over the text/abstract and amended typos and grammatical errors as much as possible to improve the manuscript more helpful to the readers.**

2. It should be clarified that fecal microbiota transplantation is identical to probiotics, timing, dose etc

**There are few literatures showing the effectiveness comparison between fecal microbiota transplantation and probiotics. This issue may be an important target of the upcoming research in this field.**

3. GVHD is generally characterized by proliferation, cytokine production and/or migration of reactive donor T cells, how to impact T cells by probiotics? Should be reviewed logically

**Probiotics could improve the composition of host gut microbiota so as to produce some beneficial metabolites including SCFAs, which could impact on the reactive T cells related to the GVHD. Regarding this, we have already mentioned in the text of section 3 as following, “Remarkably, increased production of microbiota-derived SCFAs could improve the Treg/Th17 balance [39]. In addition, elevated production of SCFAs may lead to the enhanced Treg generation and the suppressed Th17 development [40]. Moreover, SCFAs may up-regulate the production of anti-inflammatory cytokines resulting in the induction of Tregs [41]”.**

#### Reviewer 2 (05817597)

The study design of this manuscript is unclear without any paragraph mentioning on the methodology i.e. whether this manuscript is a systematic review or not? What search engine(s) and keyword(s) used? What sort of publications were included (e.g. English-only, recent 10 years etc.). This manuscript is just a bare conglomeration of some papers read without any particular scientific merit or insightful ideas. Authors would benefit from re-write of whole manuscript with clearly defined methodology, a good summary of what is known from literature, current knowledge gaps and insightful ideas.

**We believe there are many insightful ideas in our manuscript. The comments from reviewer 2 are quite different from those from the other 2 reviewers. Actually, we**

cannot respond several suggestions such as something to ensure the sort of publications included (e.g. search engine(s), English-only, recent 10 years, etc.). Is that really required for the manuscript in this journal? Please make sure the revision points which are necessary for the guideline in this journal.

Reviewer 3 (05573205)

The topic of the manuscript entitled "Advantageous tactics with certain probiotics for the treatment of graft-versus-host-disease after hematopoietic stem cell transplantation" is interesting. The manuscript is well designed and organized, and presented some original findings.

Thank you very much for the good evaluation on our manuscript.