

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 68607

Title: Effects of viremia and CD4 recovery on the gut “microbiome-immunity” axis in naïve HIV-1 patients undergoing ART therapy

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05420211

Position: Peer Reviewer

Academic degree: BSc, MPhil, MSc

Professional title: Academic Research, Research Associate, Teacher

Reviewer's Country/Territory: Pakistan

Author's Country/Territory: Italy

Manuscript submission date: 2021-05-28

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-06-11 07:05

Reviewer performed review: 2021-06-20 08:29

Review time: 9 Days and 1 Hour

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 Grade E: Do not publish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

Manuscript No.: 68607 Title: Effects of viremia and CD4 recovery on the gut “microbiome-immunity” axis in naïve HIV-1 patients undergoing ART therapy In this study, the author has studied “Effects of viremia and CD4 recovery on the gut “microbiome-immunity” axis in naïve HIV-1 patients undergoing ART therapy.” A lot of studies have already been carried out on a similar topic, and comprehensive data is available in the literature. The present manuscript investigated the fecal microbial composition, serum, and fecal microbial metabolites and serum cytokines’ profile of naïve patients before starting ART and after reaching virological suppression after 24 weeks of ART therapy. It was found that the English language used in the manuscript needs major improvements as there are some punctuation and grammatical mistakes present throughout the manuscript. The figures required the proper explanation and caption. Moreover, research models are not discussed in an understandable manner, the introduction section is poor, which reflects that the author needs a more comprehensive way of thinking. It is obvious that the quality of the manuscript does not fulfil the standards of the journal, therefore should be reconsidered after major revision. Specific comments: 1. The Abstract needs to be revised, especially the results section. 2. Please add more strong keywords. 3. Page 2: “The microbiota-immune axis springs up from a mutual interplay between human microbiota and the immune system.” Please revise the sentence, this is just like the author uses an online spinner tool to remove the plagiarism. 4. Page 3: “Converging data from many cross-sectional studies suggest that the gut microbiota (GM) changes over the progression of HIV infection [11], [12], [13], [14], [15], [16].” This is not the right way to insert so many references in one place, please omit

unnecessary references. 5. Page 3: "It is known that increased relative abundance of pro-inflammatory bacteria has been associated with increased plasma viremia." Can you please add the name of that bacteria? 6. Page 3: "It is known that increased relative abundance of pro-inflammatory bacteria..." Please merge this paragraph to the previous paragraph. 7. Page 3: "Its metabolites are also involved in regulating vital host activities." Please add few activities to support this statement. 8. Page 3: "Serum and fecal microbial metabolites and serum cytokine profile of naïve patients before starting ART..." Please make sure it is naïve or native? 9. Page 3, The whole introduction section is general. Authors are advised to revise the introduction section carefully and add more data to support the problem statement. It is advised to add literature in the introduction section to create a research gap. 10. Page 5: Total genomic DNA was extracted from frozen (-80°C) stool samples, collected at different timepoints (weeks 0, 24)..." Why was the sample not taken after every week of dose administration? 11. Page 5: "Statistical analyses on ASVs representing the bacterial community were performed in R (R Core Team, 2014) with the help of the packages phyloseq 1.26.1..." All information should be moved to at the end under the statistical analysis section. 12. Page 6: "Each sample was thawed, weighted (between 0.5-1.0 g) and added to sodium bicarbonate 10mM..." There is always a space between a unit and a value (10 mM). 13. Page 7: "Free fatty acids determination by GC-MS analysis: This heading contains repeated information, please merged with the previous heading or omit. 14. Page 7: "A value under the Low Limit of Quantification (LLOQ) was considered as 0 pg/ml." Somewhere the author use 'ml' and somewhere 'mL', please follow the same trend throughout the manuscript. 15. Page 9: ". In particular, the genera Ruminococcus 2 and Succinivibrio were ..." Please make sure that genera Ruminococcus 2 is correct. 16. Page 9: "The slight changes to the composition of the microbiome we observed (only at order and genus level) led us to ask whether the GM metabolic activity might also be changed..." Please revise the sentence. 17. Page 9:

“Did not reveal any significant change after 24 weeks of therapy for each patient (data not shown).” There is no need to mention ‘data not shown’, it decreases the worth of study. 18. Page 10: “As known, gut microbial dysbiosis is linked to aberrant immune responses ...” Can you please add more data to support this statement in relation to your results? 19. Page 10: “We documented significant changes in isobutyric ($p=0,01$), isovaleric ($p=0,04$) and 2-methylbutyric ($p=0,04$) acids ...” Please use full stop (.) between values ($p=0.01$) instead comma (,). 20. Page 11: “In order to shed the light ...” Please revise these words. 21. Page 12: “Some authors have implied that ART may enhance dysbiosis, which is consistent with the high frequency of gastrointestinal side effects with this treatment {Lozupone, 2014 #3582}, [17], [42].” Reference is missing, please correct it. 22. Page 14: There is no need to separately add a conclusion section in this type of study. It should be merged to the discussion section at the end and should be a single paragraph with key observations and strong future recommendations. 23. Authors are advised to proofread the whole manuscript to overcome grammatical mistakes. 24. Authors are advised to add a list of abbreviations. 25. The figures and table need appropriate captions. 26. The headings and subheadings need to be revised especially in results section.