Reviewer Report

Title: The unique composition of Indian gut microbiome, gene catalogue and associated faecal metabolome deciphered using multi-omics approaches

Version: Revision 1 **Date:** 11/20/2018

Reviewer name: Sean P Kenedy, Ph.D

Reviewer Comments to Author:

I commend the authors on their openness and responsiveness to the comments from both reviewers. The additional analyses performed and the clarifications in the manuscript have resulted in a much-improved draft. The availability of both the raw amplicon and WGS data in NCBI's Sequence Read Archive is a great service to the scientific community and should ensure open access to this data and its inclusion in future studies. The origin of the samples and the sequencing data is well-documented and cohort sample collection and storage appears to adhere to ethical and technical standards.

More specifically, the updated manuscript addresses and corrects all points that I raised in the first review. These include a major reanalysis of 16S data with an updated database (SILVA December 2017 versus GreenGenes 2013) and an implementation of statistical analysis with normalization performed using DESeq2. They clarify their use of downsized data for Unifrac analysis. Further, the authors now combine their data and run downstream analysis using an "Updated-IGC." This clearly aids their analysis and broadens the appeal of the manuscript as a whole. The 9% of additional genes appears to be unique to the Indian cohort. The authors also performed the suggested enterotype comparisons with the data from Arumugam et al.

Based on this new version of the manuscript, my recommendation is the manuscript can be accepted without further scientific revision. The authors should, nevertheless, have a careful review of the text to address remaining grammatical errors and awkward phrasing. A few, non-exhaustive, examples are given:

Line 114 : Change "All the recruited individuals" to "Recruited individuals"
Line 216 : Should be "relative abundances"
Line 365 : "its inward transport in microbial cells by the BCAA transporters" would be better as "its uptake by microbes via BCAA transporters"
Line 408 : Change "Though, the sequencing depth in the study was not too high..." to "Although sequencing depth was modest….longer paired-ends reads, from the cohort of 110 individuals appears sufficient to provide the first insights on the Indian gut microbiome"
Line 446 : "One aspect to this could" could be better written as "One potential explanation could be…"
Line 486 : "has known health benefits..." might be better as "has been reported to be beneficial by preventing…."
Line 505 : "are emerging, which results in the increased…." is better as "are emerging, with results showing increased….

Methods

Are the methods appropriate to the aims of the study, are they well described, and are necessary controls included? Choose an item.

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Are the conclusions adequately supported by the data shown? Choose an item.

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