

Reviewer Report

Title: Suggesting disease associations for overlooked metabolites using literature from metabolic neighbours

Version: Original Submission **Date: 2/25/2023**

Reviewer name: Biswapriya Misra

Reviewer Comments to Author:

Manuscript Number: GIGA-D-23-00014, entitled, " Suggesting disease associations for overlooked metabolites using literature from metabolic neighbours", and submitted to the journal: GigaScience, applied 'guilt by association' principle to literature information for "understudied metabolites" by using a Bayesian framework. It is an interesting manuscript, an active area of research and would have an interest in the metabolomics research community.

However, this reviewer would like to help improve the manuscript and scope of the work with the following suggestions:

1. A list/ DB of all such "overlooked metabolites" and their chemical class distribution/ ChemRICH sort of enrichment would help the readers capture the correct information.
2. How did/ would the tool perform with "very well known metabolites" for example say, phenylalanine or proline or citric acid ?
3. How does one check for "literature/ reporting biases" for the highly reported vs lowly reported metabolites in the manuscripts?
4. Does this approach distinguish for targeted vs untargeted metabolomics paper based hits ?
5. "Overlooked metabolites" need to be defined well, upfront for clarity.
6. large fraction of metabolites are rarely or never mentioned in the literature: What is a good estimate from the authors? A numerical value would be informative here.
7. Too many terms used does not help: overlooked metabolites vs. understudied metabolites and so on. Please use a singular term for consistency.
8. Method and data description section is too wordy, need to be shortened and need to use mathematical expressions whenever applicable.

Methods

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

Conclusions

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

Reporting Standards

Does the manuscript adhere to the journal's guidelines on [minimum standards of reporting?](#) Choose an item.

Choose an item.

Statistics

Are you able to assess all statistics in the manuscript, including the appropriateness of statistical tests used? Choose an item.

Quality of Written English

Please indicate the quality of language in the manuscript: Choose an item.

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