



PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 90953

Title: Immune Cell Signatures and Causal Association with Irritable Bowel Syndrome: A Mendelian Randomization Study

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 03252330

Position: Editorial Board

Academic degree: MD, MSc

Professional title: Associate Professor

Reviewer’s Country/Territory: Italy

Author’s Country/Territory: China

Manuscript submission date: 2023-12-18

Reviewer chosen by: Huo Liu

Reviewer accepted review: 2024-01-11 15:17

Reviewer performed review: 2024-01-22 17:11

Review time: 11 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" 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

The submitted paper tackles the relationship between irritable bowel disease (IBS) and the presence of some specific immunophenotypes using a Mendelian Randomization approach. The authors utilized the data obtained in the IBS GWAS study performed on the UK Biobank, as well as immunological phenotypes identified in the GWAS catalog. With this approach the authors were able to identify 9 immunophenotypes with a protective effect on IBS, whereas other 21 could increase the risk. Although the data are interesting, the paper, in the present form, could be understood only by biostatisticians and not by a wider audience. The authors should provide a “lay” description of the statistical approaches allowing the reader to understand the advantages of the methods. The first part of the results in the subsection “Investigation of the causal relationship between immunological phenotypes and IBS” is redundant and unreadable, since these results are better understood in the table form. However it is not clear why the results have been split in Figure 3 and 4 (Figure legends are identical). If the authors want to split the results it would be better do that according to protective/predisposing immunophenotype In the discussion, several sentences are not supported by references



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: office@baishideng.com
https://www.wjgnet.com

or, alternatively, the authors are quoting reviews. The original papers should be quoted. Sentences like “The Treg cell subsets marked by a level of CD25+, CD127+, CD4+, CD28-, CD45+, and CD28+ molecules were highlighted, showing significant and consistent effects on IBS. Regulatory T cells (Tregs) are pivotal in modulating immune responses and are crucial for managing inflammatory processes. Their activity is intricately linked to the human leukocyte antigen (HLA) gene 30, which can be an explanation for IBS” or “The B lymphocyte cell subsets marked by a level of CD25+, CD27+, CD24+, and CD45+ molecule, mature T cells marked by CD8+, were highlighted, as they presented top significant and consistent effects on IBS, and they had significant mediation effects to bridge the associations between other immune traits and IBS.” are extremely hypothetical, and at least they should be better explained. The sentence “Consequently, clinical and experimental evidence suggests that targeting B cells in cases of human inflammatory bowel disease (IBD) could be beneficial. The targeting of CD20, a cell surface molecule primarily found on mature B lymphocytes, by rituximab has been shown to be highly beneficial in numerous hematological and immune-mediated diseases³⁷. This may provide insight into the treatment of IBS.” is misleading.