



PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 112496

Title: Gene, Genetics and Genetic Medicines in Gastroenterology: Current status and its future

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 08099061

Position: Peer Reviewer

Academic degree and professional title: PhD, Professor

Reviewer’s Country/Territory: China

Author’s Country/Territory: India

Manuscript submission date: 2025-07-28

Reviewer chosen by: AI Editor

Reviewer accepted review: 2025-07-30 10:50

Reviewer performed review: 2025-08-11 10:58

Review time: 12 Days

Content to be reviewed	<p>Does the manuscript’s content fall within the scope of the journal? Yes</p> <p>Is there any Key Word that is not included in the manuscript title? No</p> <p>Do authors’ affiliations correspond to the content of the manuscript? Yes</p> <p>Does the Abstract contain the contents of each part of the manuscript (IMRaD)? No</p> <p>Are the Key Words complete? Yes</p>
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Is the content of the Introduction adequate? **Yes**

Is the content of the Materials and Methods complete?

Yes

Is the description of the experiments clear and complete? **Not Applicable**

Are the experimental data presented in the manuscript's biostatistics content reliable? **Not Applicable**

Are the experimental data of the Results true and reliable? **Not Applicable**

Are the quality and resolution of the images up to standard? **No**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **Yes**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Yes**

Is the content of the Discussion reasonable? **Not Applicable**

Is the Conclusion reasonable? **Yes**

Are all references necessary and reasonable? **Yes**

Do authors omit important references? **No**

Are all references related to the topic of the manuscript? **Yes**

Do authors only cite their own earlier publications? **No**

Is the manuscript's text correct, concise, and clear? **No**

Will the manuscript's content be of interest to readers?
Yes



	Are additional experiments needed for the study? No Does the research scope comply with ethics? Yes
Scientific quality	Grade C (Good)
Novelty of this manuscript	Grade D (Fair)
Creativity or innovation of this manuscript	Grade D (Fair)
Scientific significance of the conclusion in this manuscript	Grade D (Fair)
Language quality	Grade C (Good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Major revision
Re-review	No
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

This manuscript offers an encyclopedic, up-to-date overview of how genomic medicine is transforming the diagnosis, risk-stratification and treatment of gastrointestinal disorders. The breadth is impressive, spanning Mendelian syndromes, polygenic/idiopathic diseases, tumor-agnostic biomarkers, pharmacogenomics, gene therapy, emerging technologies (multi-omics, AI, organoids) and ethical issues. While



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the paper will be an extremely valuable resource for clinicians and researchers, its sheer scope has led to some structural and scientific weaknesses that should be addressed.

1. Excessive length & redundancy: The same topics—pharmacogenomics, targeted therapy, gene-delivery vectors—are reiterated in the abstract, introduction, body text, tables, and figure legends, adding an estimated 8–10 k redundant words.
2. Search strategy is described but lacks PRISMA flow diagram, inclusion/exclusion criteria, date range, or risk-of-bias assessment. Add PRISMA-compliant flowchart as supplementary Figure S1.
3. Deeply discussed but reads like a separate essay rather than integrated analysis. Condense to one balanced paragraph in main text; move expanded discussion to supplement.
4. The ethics discussion (>1,000 words) reads as a standalone essay.
5. Relies heavily on pre-clinical studies and early-phase trials; no mention of recent FDA/EMA approvals. Revise “Future Gene Therapy” section to clarify that most GI applications remain experimental.
6. Provide real-world performance data for at least one GI PRS and discuss limitations.
7. The phrase “microbial dysbiosis is the main culprit” overstates causality. Claims “microbial dysbiosis is the main culprit” in IBS; this overstates causality. Rephrase to “associated with” and cite Cochrane review showing modest effect sizes for microbiome-directed therapies.
8. The review is highly encyclopedic rather than hypothesis-driven.
9. Figure 1 & 2 are informative but font sizes are too small for print. Supply high-resolution vector graphics.
10. This manuscript is an impressive, encyclopedic compendium of gastrointestinal (GI) genomic medicine, but its “everything-included” approach has generated information overload and redundancy. Addressing these points will transform an exhaustive catalog



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into a concise, high-impact review suitable for a leading gastroenterology or genetics journal.



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Reviewer’s code: 05754263

Position: Peer Reviewer

Academic degree and professional title: Chief Physician, MD, Professor

Reviewer’s Country/Territory: China

Author’s Country/Territory: India

Manuscript submission date: 2025-07-28

Reviewer chosen by: Jia-Lin Zhang

Reviewer accepted review: 2025-08-15 10:01

Reviewer performed review: 2025-08-25 11:08

Review time: 10 Days and 1 Hour

Content to be reviewed	<p>Does the manuscript’s content fall within the scope of the journal? Yes</p> <p>Is there any Key Word that is not included in the manuscript title? No</p> <p>Do authors’ affiliations correspond to the content of the manuscript? Yes</p> <p>Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes</p> <p>Are the Key Words complete? Yes</p>
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Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **Yes**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Yes**

Is the content of the Discussion reasonable? **Yes**

Is the Conclusion reasonable? **Yes**

Are all references necessary and reasonable? **Yes**

Do authors omit important references? **No**

Are all references related to the topic of the manuscript? **Yes**

Do authors only cite their own earlier publications? **No**

Is the manuscript's text correct, concise, and clear? **No**

Will the manuscript's content be of interest to readers? **Yes**

Are additional experiments needed for the study? **Yes**



	Does the research scope comply with ethics? Yes
Scientific quality	Grade B (Very good)
Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade C (Good)
Scientific significance of the conclusion in this manuscript	Grade B (Very Good)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Major revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

This review addresses a cutting-edge topic with comprehensive content, systematically reviewing the research advances and clinical translational applications of genetics and genomic medicine in the field of gastroenterology. The article is well-supported by data and rich in references, covering a complete chain from basic mechanisms (germline/somatic mutations, epigenetics) to cutting-edge technologies (CRISPR, multi-omics, AI), and further to clinical practice (genetic testing, targeted therapy,



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genetic counseling) and ethical considerations, possessing significant academic value and clinical reference importance. The main framework of the article is reasonable, but certain issues exist in organizational structure, content depth, precision of expression, and timeliness, as detailed below:

1.The structure and organizational logic are unclear: The article covers a wide range of content, but the sections primarily rely on content stacking, and multi-level headings are not used to distinguish primary and secondary points, resulting in an unclear flow that makes it difficult for readers to quickly grasp the overall framework. Additionally, some content repeats (e.g., genetic testing technology is introduced multiple times in different sections), making the article redundant. It is recommended to add hierarchical headings to clarify the logical relationships between sections and merge similar content to enhance coherence.

2.The language and expression are not concise: Some sentences are lengthy and repetitive, with loose logic. It is recommended to break down long sentences, optimize the use of logical connectors, and eliminate repetitive expressions to increase information density.

3.The chart titles and annotations are insufficiently clear: Some tables are overly large (e.g., Table 4), resulting in information overload that hinders readers' extraction of key information. It is recommended to split large tables (e.g., Table 4) by disease type (e.g., genetic syndromes, inflammatory diseases, malignant tumors, metabolic diseases) or provide summary tables.

4.Some content is missing: For example, clinical genetic testing is classified into three types based on origin: germline variation, somatic variation, and mosaic variation. The article does not discuss mosaic variation, which also holds important value in gastrointestinal and HPB diseases. It is recommended to supplement this.

5.The content depth and timeliness are insufficient: The discussion of the artificial



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intelligence section is relatively general. It is recommended to add 1–2 specific cases.

6.Lack of clinical guidance: It is recommended to indicate in sections such as "targeted therapy" and "gene therapy" which treatments have been approved by the FDA/NMPA (e.g., NTRK inhibitor larotrectinib) and which are in Phase III clinical trials (e.g., KRAS G12C inhibitors) to enhance clinical guidance.

7.The ethical discussion is somewhat generalized: It is recommended to conduct an in-depth analysis based on specific cases in gastroenterology (e.g., racial bias in PRS for IBD risk prediction) to enhance pertinence and practical significance.