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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 115009

Title: Molecular profiling-directed individualized adjuvant therapy in colorectal cancer: Bridging consensus guidelines to clinical disparities

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 08347911

Position: Peer Reviewer

Academic degree and professional title: PhD

Reviewer's Country/Territory: South Africa

Author's Country/Territory: China

Manuscript submission date: 2025-10-05

Reviewer chosen by: Hong-Xin Jiang

Reviewer accepted review: 2025-10-22 09:05

Reviewer performed review: 2025-10-22 09:39

Review time: 1 Hour

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

Is the content of the Materials and Methods complete?

Not Applicable

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**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Not Applicable**

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? **Not Applicable**

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**

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**



	Are the quality and resolution of the images up to standard? Not Applicable Is the manuscript's text correct, concise, and clear? Yes
Scientific quality	Grade A (Excellent)
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	Minor 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

i) Keywords

The keywords are relevant and effectively reflect the manuscript's focus areas. Add: "Consensus Molecular Subtypes (CMS)"

ii) Abstract



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The abstract is acceptable and logically structured. It aligns well with the manuscript's structure. Include a clearer statement of the review methodology (e.g., database search or inclusion criteria).

iii) Contents Adequacy

The manuscript is comprehensive and well-organised. The progression from molecular biomarkers to systemic solutions maintains scientific coherence. Possibly review Sections 2.4 and 4.1, removing some duplication between single-cell/spatial omics descriptions and multi-omics integration under "Technological Innovation."

iv) Materials and Methods

A Review article. Add a short paragraph detailing search strategy (databases, inclusion/exclusion criteria, and time range) to enhance reproducibility and scientific rigour.

v) Description of Experiment

Not applicable since this is not an experimental study.

vi) Experimental Data Reliability

The review draws from high-quality, peer-reviewed sources.

The interpretation of data appears scientifically sound and balanced. No misrepresentation or overstatement of trial outcomes was detected.

vii) Duplication Between Sections

Check the following for minor thematic overlap between:

- o Section 2.3 (ctDNA) and Section 3.3 (Dynamic Monitoring).
- o Section 2.4 (Single-cell/spatial omics) and Section 4.1 (Multi-omics Integration).
- o Recommendation: Merge or cross-reference these sections to reduce redundancy and improve conciseness.

viii) Discussion

The discussion is comprehensive. The "Bridging the Gap" section is well articulated.



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Clearly distinguish evidence gaps (what is unknown) from implementation barriers (what is known but not applied).

ix) Conclusion

The conclusion is acceptable and aligns with the stated objectives. Include a paragraph on key actionable recommendations.

x) Need for Additional Experiments

No direct experiments are required. However, the author could propose prospective validation studies for integrated AI-omics decision tools and ctDNA-guided interventions in the adjuvant setting.

xi) Reference Quality and Completeness

The reference list is extensive, including seminal and recent works.

Check for reference consistency

Overall Evaluation

This manuscript demonstrates strong scientific merit and contributes meaningfully to bridging precision oncology research with practical implementation in colorectal cancer adjuvant therapy.

It is publication-ready after minor structural and methodological clarifications.



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Reviewer's code: 08353619

Position: Peer Reviewer

Academic degree and professional title: Chief Nurse, Dean, Deputy Director, Professor, Research Fellow

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2025-10-05

Reviewer chosen by: Hong-Xin Jiang

Reviewer accepted review: 2025-10-29 00:34

Reviewer performed review: 2025-11-03 13:41

Review time: 5 Days and 13 Hours

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? Yes Is there any Key Word that is not included in the manuscript title? Yes Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes
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Conclusion	Minor 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

Cheng (2025) presents a timely and well-argued narrative review on molecular profiling-directed individualized adjuvant therapy in colorectal cancer, aiming to bridge consensus guidelines with real-world implementation gaps across testing, decision-making, and policy levels. The manuscript synthesizes key biomarkers such as



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dMMR/MSI, RAS/RAF, CMS/CRIS, and ctDNA, and proposes an integrated algorithm and a forward-looking framework for dynamic, risk-adapted care. These contributions fill a practical gap by coupling molecular science with pathway engineering and health-system levers, and the figures reinforce the translational emphasis.

First, the review would benefit from greater methodological transparency befitting a state-of-the-art narrative synthesis. Please add a brief Methods paragraph describing how the literature was identified and appraised: databases searched, date limits, language restrictions, core inclusion priorities (adjuvant setting, perioperative trials, real-world evidence), and how conflicting evidence was reconciled. Because several recommendations hinge on the distinct roles of prognostic versus predictive biomarkers, the paper should also standardize evidence labeling in text, tables, and figures. For example, ctDNA is positioned as a driver of adaptive therapy, yet current guidelines largely confine its use to trial contexts; a compact table listing assay types, timing windows, positivity thresholds, and performance metrics would sharpen claims and help clinicians interpret platform variability.

Second, the framing of evidence in the adjuvant context should be calibrated at a few key junctures to avoid inadvertent overstatement. The Figure 1 legend currently implies that MSI-H/dMMR patients are “eligible for adjuvant immunotherapy,” whereas mature phase III outcomes in the adjuvant setting remain emergent and practice is heterogeneous; rephrase to emphasize clinical-trial prioritization and explicitly separate neoadjuvant, adjuvant, and metastatic extrapolations throughout. Where trials such as ATOMIC and DYNAMIC are cited, please summarize outcomes with effect sizes and uncertainty where available, or clearly mark them as pending if results are preliminary in this version. Finally, given the paper’s important section on access and economics, consider adding one paragraph on transferability to resource-constrained settings with concrete levers (coverage of core testing, tiered algorithms when CMS/CRIS are



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unavailable, ctDNA cadence options) and aligning Figure 2 with those tiers so the workflow is implementable in diverse environments.

In summary, this is a valuable, practice-oriented review with clear clinical utility. With the addition of a brief Methods description, a ctDNA summary table, careful rewording around adjuvant-specific evidence, and minor alignment between text and figures, the manuscript will be stronger and more precise without changing its scope. I recommend minor revision.