

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastrointestinal Oncology*

**Manuscript NO:** 80448

**Title:** Challenges to addressing the unmet medical needs for immunotherapy targeting cold colorectal cancer

**Provenance and peer review:** Invited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05743795

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** South Korea

**Manuscript submission date:** 2022-09-28

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-11-08 00:23

**Reviewer performed review:** 2022-11-09 08:28

**Review time:** 1 Day and 8 Hours

Scientific quality	<input checked="" type="checkbox"/> Grade A: Excellent <input 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 Grade E: Do not publish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 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 type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

Cold colorectal cancer is currently a challenge in the field of CRC treatment, especially in the field of immunotherapy. How to solve these problems has become a hot topic of basic and clinical research, including the transformation of cold cancer into hot cancer, and the stimulation of T-cell killing. In this article, the author introduced the concept of cold colorectal cancer (CRC) and various strategies across non-clinical and clinical for enhancing immunotherapeutic efficacy and further encourages the journey to an advanced level of immunotherapies targeting cold CRC. This article provided a detailed and systematic review of the latest research and clinical implementation progress in the field of cold colorectal cancer, giving us a comprehensive understanding and inspiration to help the direction of research clinical translation to find.

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastrointestinal Oncology*

**Manuscript NO:** 80448

**Title:** Challenges to addressing the unmet medical needs for immunotherapy targeting cold colorectal cancer

**Provenance and peer review:** Invited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 04163041

**Position:** Editorial Board

**Academic degree:** FACS, MBBS, MNAMS

**Professional title:** Professor

**Reviewer's Country/Territory:** India

**Author's Country/Territory:** South Korea

**Manuscript submission date:** 2022-09-28

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2022-11-29 07:55

**Reviewer performed review:** 2022-12-08 15:17

**Review time:** 9 Days and 7 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" 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 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 type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<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
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	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 topic chosen falls short of portraying the complexity of the issue handled. The subject “immunotherapy of CRC management” is current hot topic and kindles the readers’ enthusiasm. Immunotherapy resistance is complex and multifaceted, not only depended on tumor factors but also on the dynamic intensively explored tumor micro environment. The authors review this in Colorectal cancer and describes immunotherapy resistance by cold, immune-desert, tumor. The tumour factors contributing to resistance is only tip of the iceberg, and an attempt has been made to refer to multiple studies to portray the current level of understanding, though more than 2000 trails are currently in progress on PD -1 & Anti PD -L1 targeted drug itself. The concept of dividing the strategies to clinical and non clinical strategies targeting cold tumors is complex to comprehend. To conclusion drawn viz. “immunotherapies’ failure is due to non immunogenic characteristics of cold CRC” oversimplifies the immensely complex perplexing problem. The write up is too long for an ediorial.

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastrointestinal Oncology*

**Manuscript NO:** 80448

**Title:** Challenges to addressing the unmet medical needs for immunotherapy targeting cold colorectal cancer

**Provenance and peer review:** Invited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05774529

**Position:** Editorial Board

**Academic degree:** FASCRS, MD, PhD

**Professional title:** Deputy Director

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** South Korea

**Manuscript submission date:** 2022-09-28

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2022-11-29 12:43

**Reviewer performed review:** 2022-12-11 00:08

**Review time:** 11 Days and 11 Hours

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 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 type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	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

Thank you for giving me the opportunity to review this manuscript. Immunotherapy is a hot topic in the field of cancer therapy. This is a very meaningful but complex topic. pMMR/MSS mCRC does not respond well to immunotherapy. It is important to explore immunotherapies that can benefit such subtype of patients. 1. Structurally, this manuscript is more like a review. 2. The language of the manuscript should be improved.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

**Name of journal:** *World Journal of Gastrointestinal Oncology*

**Manuscript NO:** 80448

**Title:** Challenges to addressing the unmet medical needs for immunotherapy targeting cold colorectal cancer

**Provenance and peer review:** Invited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 04163041

**Position:** Editorial Board

**Academic degree:** FACS, MBBS, MNAMS

**Professional title:** Professor

**Reviewer's Country/Territory:** India

**Author's Country/Territory:** South Korea

**Manuscript submission date:** 2022-09-28

**Reviewer chosen by:** Jing-Jie Wang

**Reviewer accepted review:** 2022-12-19 16:17

**Reviewer performed review:** 2022-12-20 17:50

**Review time:** 1 Day and 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Peer-reviewer</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

**statements**Conflicts-of-Interest: [ ☐ ] Yes [ ☒ ] No**SPECIFIC COMMENTS TO AUTHORS**

I note that no revision has been done to the article. The editorial focuses mainly on converting cold into hot tumor, by molecular and therapeutic strategies, but fails to impress whether it is for early-stage CRC or metastatic disease. The conclusion lacks punch and fails to synopsise the strategies to compassing to hot tumour. It withers direction to optimal model to human immune system. Use of gut microbiome, role of nano technology in CRC immune modulation are not alluded to. So also, it fails to insinuate the possible biomarkers that may be reckoned with. Nor it warns about immunotherapy related harm to the patient.