Baishideng Publishing Group

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

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 71964

Title: Colorectal cancer carcinogenesis: From bench to bedside

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: Portugal

Manuscript submission date: 2021-09-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-09 01:49

Reviewer performed review: 2021-10-09 02:52

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

Baishideng Publishing Group

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

statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In this review, the author systematically summarizes the value of molecular and genetic features in early screening, diagnosis, therapeutic strategy and prognostic implications for CRC patients. This review covers almost all of the important CRC carcinogenesis related molecular and mutation features, including MSI, BRAF, KRAS, APC and TILs. In my opinion, it is a good review with great data integrity and scientific rigor. However, this article also has some areas desired for improvement: 1. We all know that EGFR mutation is an important tumor inducer and therapeutic target for CRC. Could the author please supplement the relevant content of EGFR in this article? 2. The conclusion part is too simple. Many conclusive statements that appear in the results section should appear in the conclusions.

Baishideng Publishing Group

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

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 71964

Title: Colorectal cancer carcinogenesis: From bench to bedside

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05775860
Position: Editorial Board
Academic degree: PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Portugal

Manuscript submission date: 2021-09-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-11 00:54

Reviewer performed review: 2021-10-13 06:55

Review time: 2 Days and 6 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

Baishideng Publishing Group

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

statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The manuscript entitled, "Colorectal cancer carcinogenesis: bench-to-bedside", reports a review on genetic factors involved in CRC carcinogenesis. The authors summarized the carcinogenesis pathways and key genes that play roles in CRC development and treatment. The manuscript is informative and may draw attentions of readers who are interested in the field. The below lists some suggestions that the authors may consider. 1. "In 1990, Fearon and Vogelstein published an important paper about colorectal carcinogenesis." , a reference should be added for this sentence. 2. "the "hypermutated" (more than 12 mutations per 106 bases) and the "non-hypermutated"", there should be a definition for the "non-hypermutated" tumors as well. What is the percentage threshold for mutations to be considered as "non-hypermutated". 3. When Figure 1 was mentioned for the first time, only part of the information provided by Figure 1 was summarized. In this paragraph, it will be better if the authors can give a full introduction of contents proposed in Figure 1. 4. "Characterized by a phenotype of DNA hypermethylation at specific regulatory sites (CpG islands) in the promoter regions of genes – the CIMP.", need a reference here. 5. The English grammar needs to be checked again, e.g. "these data seems interesting".

Baishideng Publishing Group

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

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 71964

Title: Colorectal cancer carcinogenesis: From bench to bedside

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05469314
Position: Editorial Board
Academic degree: MD, PhD

Professional title: Doctor, Research Assistant Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Portugal

Manuscript submission date: 2021-09-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-14 11:19

Reviewer performed review: 2021-10-17 03:25

Review time: 2 Days and 16 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer	Peer-Review: [ ] Anonymous [Y] Onymous

Baishideng Publishing Group

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

statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This is an applicable review. With the theme of bench-to-bedside, this paper presents the current research progress of colorectal cancer. General comments: 1. Recent advances in basic research of colorectal cancer need to be supplemented, such as immune-related regulation, intestinal flora, etc. 2. Biomarkers for colorectal cancer screening need to be further introduced. More novel biomarkers can be supplemented, including cfDNA, exosomes, etc.

Baishideng Publishing Group

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

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 71964

Title: Colorectal cancer carcinogenesis: From bench to bedside

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05775440
Position: Peer Reviewer
Academic degree: PhD

Professional title: Associate Research Scientist

Reviewer's Country/Territory: China

Author's Country/Territory: Portugal

Manuscript submission date: 2021-09-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-11 01:00

Reviewer performed review: 2021-10-19 02:58

Review time: 8 Days and 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

Baishideng Publishing Group

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

statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

1 Title. Does the title reflect the main subject/hypothesis of the manuscript? YES 2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? YES 3 Key words. Do the key words reflect the focus of the manuscript? YES 4 Background. Does the manuscript adequately describe the background, present status and significance of the study? YES 5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? YES 6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? YES This review gives us a reminder about the careful use of PPI in CRC. 7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? YES, YES, YES 8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends? YES 9 Biostatistics. Does the manuscript meet the requirements of biostatistics? YES 10 Units. Does the manuscript meet the requirements of use of SI units? YES 11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? YES, NO 12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and

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

appropriate? YES 13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting? YES 14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? YES

Baishideng Publishing Group

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

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 71964

Title: Colorectal cancer carcinogenesis: From bench to bedside

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05469117
Position: Editorial Board
Academic degree: PhD

Professional title: Adjunct Professor, Chief Physician, Deputy Director

Reviewer's Country/Territory: China

Author's Country/Territory: Portugal

Manuscript submission date: 2021-09-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-15 09:57

Reviewer performed review: 2021-10-23 18:19

Review time: 8 Days and 8 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

Baishideng Publishing Group

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

statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Thank you for giving me a chance to review this research regarding Colorectal cancer carcinogenesis.My major comments are as follows: 1.The reference format is inconsistent. For example, reference18 does not provide doi （https://doi.org/10.1007/s11725-017-0730-2).According to this paper, CRC was marked into four CMSs with distinguishing features: CMS1 (microsatellite instability immune, 14%)， CMS2 (canonical, 37%), CMS3 (metabolic, 13%), and CMS4 (mesenchymal, 23%)，There must be a problem with the proportions in Figure 1. (CMS1 vs CMS3). 2.Page6, line 6:" characterized by a hypermutated phenotype in the absence of MSI ,"the absence of" may be inappropriate used. 3.Page11, line 5:"KRAS exons 3 and 4 mutations (as the less common NRAS exons 2, 3 and 4 mutations) have been shown to be associated to an intrinsic resistance to anti-EGF antibodies (cetuximab and panitumumab),"we want to know wether KRAS exons 2 mutations is associated to an intrinsic resistance to anti-EGF antibodies ?