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 Gastroenterology*

Manuscript NO: 80222

Title: Application of nanotechnology in reversing therapeutic resistance and controlling metastasis of colorectal cancer

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03004840
Position: Editorial Board
Academic degree: MSc, PhD
Professional title: Academic Research, Postdoc, Senior Researcher
Reviewer's Country/Territory: Turkey
Author's Country/Territory: China

Manuscript submission date: 2022-09-25

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-10-14 19:40

Reviewer performed review: 2022-10-25 20:34

Review time: 11 Days

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This review article summarizes the resistance mechanisms for chemotherapy, radiotherapy, immunotherapy, and targeted therapy alternatives used in colorectal cancer. Additionally, recent advances in nanotechnology in CRC therapy were assessed in terms of therapeutic resistance and preventing metastasis in this review paper. Overall paper is well written and intellectually sound, however it could be improved by expanding on a few points and providing more details. Below are suggestions for improving the manuscript. 1. Pharmacokinetic effects (absorption, distribution, metabolism and elimination) can also limit the amount of drug which reaches the tumor. Authors are requested to make mention of the pharmacokinetic effects in the chemotherapy resistance section of the manuscript. 2. The phosphatidylinositide-3-kinase (PI3K)/proteinkinase B (Akt) pathway is one of the well known pathway for the development and progression of many solid cancers. PI3K signalling and its downstream effector Akt are considered one of the important reasons of chemoresistance in colorectal cancer therapy. The reviewers should additionally mention the PI3K/AKT/mTOR signalling pathway importance in the chemotherapy resistance section of the manuscript. 3. Recent studies have also showed a link between chemotherapy resistance and the epithelial–mesenchymal transition (EMT) phenotype. Authors indicated that the importance of the EMT for radiotherapy resistance. Please, give a detail for the EMT-chemotherapy resistance link and also the other resistance types. 4. Hypoxia has a crucial role in radiotherapy resistance and it could be a cause for treatment failure after radiotherapy. The role of hypoxia in radiotherapy resistance should be addressed in the related part of the manuscript. 5. The authors should also

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

mention Anti-VEGF alternative for the CRC therapy and resistance problem in the targeted therapy resistance section of the manuscript. 6. Recently, extracellular vesicles (EVs), a heterogeneous group of vesicles involved in cell-to-cell communication, have been shown to contribute to drug therapy resistance as crucial modulators in a variety of cancer. The importance and role of EVs in therapy resistance for cancer should be addressed throughout the manuscript. 7. Exosome has been reported as an important potential system that could be effectively used as a bioinspired, bioengineered, and biomimetic drug delivery solution considering its toxicity, immunogenicity, and rapid clearance by the mononuclear phagocyte system. Exosome-mimetic vesicles are receiving much interest for developing nano-sized delivery systems 8. Recently, exosomes, one of the important subgroup of EVs, have been proposed as an important potential system that might be effectively used for drug delivery solution. They have advantages and disadvantages compared to liposomes and nanoparticles. Authors are requested to mention to exosomes as an alternative for drug delivery solution in this review article. 9. Resolution of figure 1 is not good. White color shouldn't be preferred in the text of the figure.

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 Gastroenterology*

Manuscript NO: 80222

Title: Application of nanotechnology in reversing therapeutic resistance and controlling metastasis of colorectal cancer

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05743300
Position: Peer Reviewer
Academic degree: PhD
Professional title: Honorary Research Fellow
Reviewer's Country/Territory: Czech Republic
Author's Country/Territory: China

Manuscript submission date: 2022-09-25

Reviewer chosen by: Dong-Mei Wang

Reviewer accepted review: 2022-12-01 12:53

Reviewer performed review: 2022-12-01 15:41

Review time: 2 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) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

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-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

N/A

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

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 80222

Title: Application of nanotechnology in reversing therapeutic resistance and controlling metastasis of colorectal cancer

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03004840
Position: Editorial Board
Academic degree: MSc, PhD

Professional title: Academic Research, Postdoc, Senior Researcher

Reviewer's Country/Territory: Turkey

Author's Country/Territory: China

Manuscript submission date: 2022-09-25

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-02-11 20:43

Reviewer performed review: 2023-02-11 21:02

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] 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	[Y] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
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 authors have satisfactory improved their paper, in reaction to the comments. I would like to thank the authors for their great efforts.