PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 58796

Title: The pathological significance of abnormal RON and PD- Y expression in colorectal cancer

Reviewer's code: 05128663

Position: Peer Reviewer

Academic degree: BSc, MD, MSc, PhD

Professional title: Academic Research, Attending Doctor, Postdoc, Research Associate, Research Fellow

Reviewer's Country/Territory: Greece

Author's Country/Territory: China

Manuscript submission date: 2020-08-09

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-08-09 16:41

Reviewer performed review: 2020-08-15 16:59

Review time: 6 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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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

SPECIFIC COMMENTS TO AUTHORS

The article with the title "The pathological significance of abnormal RON and PD-L1 expression in colorectal cancer" is in generally well done, but I would offer these comments to the investigators: 1) Figure 6. I highly recommend to check also downstream agents of AKT such as mTOR, ps6r etc. 2) i) Figure 6 A. The authors identified the activation of the signaling pathways MEK/ERK and AKT/mTOR. Both pathways are regulators of autophagy, a significant mechanism for several cellular processes including the emerging role of autophagy in shaping the crosstalk between the cancer cells and the tumor microenvironment and PD-L1 expression in cancer cells. I recommend the authors to perform an experiment in order to identify the levels of autophagy markers such as LC3II, p62, Beclin-1.   You can discuss the possible correlation between authophagy activation and PD-L1 expression.   Koustas E, et al. PLoS One. 2018;13(11):e0207227. doi: 10.1371/journal.pone.0207227. Koustas E, et al. Cancers (Basel). 2019;11(4):533 doi: 10.3390/cancers11040533. ii) If autophagy is activated, an autophagy inhibitor such as Hydroxychloroquine will reveal a possible mechanism of action for your model. 3) It is properly to mention that the antibody against p-AKT detects the endogenous levels of Akt only when phosphorylated at Ser473. Because the complicate mechanisms of PI3K/AKT/mTOR axis activation with the positive feedback loop (AKTthr308, ser473, mTOR1 and mTOR2) on autophagy, I believe that it will be useful to discuss it. 4) All sections need to be revised to take into account all revisions made.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 58796

Title: The pathological significance of abnormal RON and PD- Y expression in colorectal cancer

Reviewer's code: 05275248

Position: Peer Reviewer

Academic degree: PhD

Professional title: Associate Researcher

Reviewer's Country/Territory: China

Author's Country/Territory: China

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Review time: 6 Days and 7 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) [ ] Minor revision　[Y] Major revision　[ ] Rejection
Re-review	[Y] Yes　[ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous　[ ] Onymous Conflicts-of-Interest: [ ] Yes　[Y] No

SPECIFIC COMMENTS TO AUTHORS

1. The section of patient demographics in Results should be shown in M&M, and "Expression patterns of RON and PD-L1 in the GEO cohort" should be described in detail. 2. In general, authors should use more than 2 cell lines to validated their findings in in vitro experiments. I am puzzled why LoVo cells with lower toxicity was not used, which appeared in Supplemental. 3. It is unreasonable for authors to assess the relationship between RON and PD-L1 by a multiplex immunofluorescence staining. They should use quantitative assays such as RT-PCR and ELISA, etc. 4. Fig 3c which should be replaced by new one is too difficult to distinguish; 5. The number of cells is too few in Fig 5a; Phosphorylated RON should also detected in Fig 5b. The picture quality of PD-L1 in Fig 5b should be improved. 6. Authors should supply with some information and intention in this study of inhibitor MSP.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors have revised the manuscript in accordance with comments.