

PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 72736

Title: Identification of circ_0000375 and circ_0011536 as novel diagnostic biomarkers of colorectal cancer

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05776245

Position: Peer Reviewer

Academic degree: BSc, MSc

Professional title: Academic Research, Research Scientist, Teaching Assistant

Reviewer's Country/Territory: Poland

Author's Country/Territory: China

Manuscript submission date: 2021-10-29

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-29 17:06

Reviewer performed review: 2021-10-31 09:40

Review time: 1 Day and 16 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 Grade E: Do not publish
Language quality	<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
Conclusion	<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
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	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

Dear Authors, great work in preparing solid research focused on novel CRC biomarkers being circRNAs. Revealing the binding sites for circ0000375- miR1182 and circ0011536-miR1246 is also highly appreciated. There is a room for improvement hence please answer or consider the following:

1. Add hyphen between “miRNA” and “binding” in second paragraph of Introduction.
2. Consider changing the last sentence of Introduction: delete “that” and change “CRC and provided” to “CRC, providing”.
3. Could you please clarify why RKO cells were not subjected to transfection and not investigated throughout the study the same as HCT116 and SW480?
4. What threshold was used for differential expression analysis visible in Figure 1A? Could this be enclosed? I am interested in fold-change and p-value. This should be included in Materials and Methods.
5. Consider standardizing the visualization of statistical significance – “a/b/c” symbols (representing $P < 0.001$; $P < 0.01$; $P < 0.05$, respectively) are either above the specific bar (Fig1E or F) or between bars (above the line; Figure 1B or C). I would suggest to use the latter method in all figures.
6. Could you please explain what the inward and outward arrows mean in Figure 2A and B?
7. In supplementary table 3, is number “1” means “true”, confirming that the mRNA from specific gene was identified in the database as target for each miRNA?
8. Please double-check whether all gene symbols are italicized. I spotted “TP53” symbol not italicized in Discussion.

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Title: Identification of circ_0000375 and circ_0011536 as novel diagnostic biomarkers of colorectal cancer

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03491790

Position: Editorial Board

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: Thailand

Author's Country/Territory: China

Manuscript submission date: 2021-10-29

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-11-19 04:20

Reviewer performed review: 2021-11-19 07:06

Review time: 2 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
Language quality	<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
Conclusion	<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
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No
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SPECIFIC COMMENTS TO AUTHORS

The manuscript describes the possible role of circ_0000375 and circ_0011536 as tumor suppressors in CRC progression, providing novel biomarkers for CRC diagnosis and promising candidates for therapeutic exploration. The contents presented herein are scientifically sound. However, there are points that the authors should address as follows. 1. Fig. 1, the authors should indicate both circ_0000375 and circ_0011536 in Fig. 1A. What rationale of choosing these two circRNAs for further study? What about other circRNAs with high fold change and confidence? 2. For wound healing assay, did the authors use TScratch to quantify the migrating areas? 3. Fig 4 and 5 can be combined as they represent the same results but in different cell lines. 4. Have the authors performed the analysis based on both circRNAs? ie. will both yield better ROC or diagnosis power compared to each single one? 5. Table 2, are the survival data available? If so, the authors should perform survival plots based on these two circRNAs.