

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Surgery*

Manuscript NO: 86056

Title: Comparative detection of syndecan-2 (SD) methylation in preoperative and postoperative stool DNA in patients with colorectal cancer

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02567654

Position: Peer Reviewer

Academic degree: MD

Professional title: Assistant Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: South Korea

Manuscript submission date: 2023-06-08

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-06-25 13:18

Reviewer performed review: 2023-07-03 15:41

Review time: 8 Days and 2 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 Grade E: Do not publish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 checked="" 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 checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation
Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<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
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="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors have measured methylated SDC2 from stool samples in patients with colon cancer before and after surgical treatment. The pre-operative sensitivity was 88.6%. Sensitivity was less for early-stage disease. The post-operative test positivity rate was about 20%, higher in women. None of these false positives had recurrence. Of the 6 recurrences in 46 months of follow up, none were SDC2 positive in the post-operative sample. The data indicate that the source of SDC2 in the pre-operative sample was likely of tumor origin. The authors concluded that these observations support a use case of methylated SDC2 in post-operative surveillance. However, the impact of this application is likely low due to the high post-operative false positive rate and a lack of prediction of recurrence. It therefore seems highly unlikely that SDC2 methylation would disrupt surveillance colonoscopy for CRC survivors, who remain at risk for advanced pre-cancers, metachronous new CRC, and less often recurrence of the primary cancer. Study

strengths include: • Relatively large sample size (104 patients) • Clear study flow diagram (Fig 1) • Clear definitions of positive and negative test thresholds Addressable weaknesses include: • Lack of 95% confidence intervals around sensitivity and specificity estimates • Blank STROBE checklist (should indicate where in the manuscript the items are reported) • Missing X- and Y- axis values and legend for Fig 2 • Reporting of blinding for laboratory test operators • Lack of clear statement of involvement of Genomictree, Inc by whom 2 of the authors are employees and who markets a methylation-based CRC screening test

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Reviewer's code: 02567654

Position: Peer Reviewer

Academic degree: MD

Professional title: Assistant Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: South Korea

Manuscript submission date: 2023-06-08

Reviewer chosen by: Han Zhang

Reviewer accepted review: 2023-07-17 13:24

Reviewer performed review: 2023-07-17 13:34

Review time: 1 Hour

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 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
Conclusion	<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
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [☒] Yes [☐] No

SPECIFIC COMMENTS TO AUTHORS

The authors have responded to all points in my initial review.