



## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastrointestinal Oncology*

**Manuscript NO:** 87680

**Title:** High PNPLA8 expression as a biomarker for poor prognosis of colorectal cancer

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 03479334

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Chief Physician

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-08-22

**Reviewer chosen by:** Yu-Lu Chen

**Reviewer accepted review:** 2023-09-28 23:41

**Reviewer performed review:** 2023-10-09 10:36

**Review time:** 10 Days and 10 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input checked="" type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<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 novelty
<b>Creativity or innovation of this manuscript</b>	<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 creativity or innovation



<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input checked="" type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	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**

This is a retrospective study with PNPLA8 expression as a biomarker for poor prognosis of colorectal cancer. I have the following comments. 1) The authors described that the median follow-up time of the patient cohort was 46.1 months. What was the actual range of follow-up periods? Please give the shortest and longest follow-up periods. 2) The study is listed as running from May 2008 to November 2012, which is more than 10 years ago. It's hard to say because we don't know the longest follow-up period, but even if that's the case, the cases studied are old.



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**Peer-review model:** Single blind

**Reviewer's code:** 05263678

**Position:** Associate Editor

**Academic degree:** FACS, MD, PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** United States

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-08-22

**Reviewer chosen by:** Yu-Lu Chen

**Reviewer accepted review:** 2023-10-31 15:40

**Reviewer performed review:** 2023-10-31 16:02

**Review time:** 1 Hour

<b>Scientific quality</b>	<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
<b>Novelty of this manuscript</b>	<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 novelty
<b>Creativity or innovation of this manuscript</b>	<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 creativity or innovation



<b>Scientific significance of the conclusion in this manuscript</b>	<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
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	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**

This interesting study identifies PNPLA8 immunoreactivity as a possible prognostic factor for colorectal cancer. 1. The manuscript would benefit from review and editing by a native English speaker. 2. In the paragraph on “correlations between PNPLA8 expression and clinicopathological parameters”, the third sentence beginning “These samples were categorized...” suggests that only the 689 specimens with some PNPLA8 expression were categorized into low and high expressers and compared. However, table 2 suggests that all were compared (presumably categorizing the low expression and zero expression together. This should be categorized. 3. What does it mean to say that 751 were successfully stained? Were there other tissue blocks that were not successfully stained and thus discarded from the study? If so, how many? 4. The last sentence of paragraph 1 of the discussion is an overstatement. These results do suggest that PNPLA8 may be prognostic, but there are no data presented here to suggest a functional role in carcinogenesis or disease progression. 5. Why do the authors think that this is not relevant for right sided colon cancer? 6. How was informed consent obtained from patients in this retrospective study? Please clarify. 7. What was the minimal,



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median, and longest follow up? How were these patients followed? How many were lost to follow up and how was their data handled? 8. The authors indicate that this has previously been implicated as a marker for colon cancer in other studies. What is the novelty here?



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**Reviewer's code:** 05330707

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Assistant Professor, Doctor

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-08-22

**Reviewer chosen by:** Yu-Lu Chen

**Reviewer accepted review:** 2023-11-09 06:42

**Reviewer performed review:** 2023-11-18 23:19

**Review time:** 9 Days and 16 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<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 novelty
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<b>Scientific significance of the conclusion in this manuscript</b>	<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
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	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**

1. There were two major problems with this study: first, the number of patients studied was small, and second, PNPAL8 expression was evaluated only by immunohistochemistry. The authors should investigate PNPAL8 expression in colorectal cancer using TCGA and other databases. 2. The authors should evaluate PLA2G6 (GVI; PLA2; INAD1; NBIA2; iPLA2; NBIA2A; NBIA2B; PARK14; PNPLA9; CaI-PLA2; IPLA2-VIA; iPLA2beta), not PNPAL8(MMLA; IPLA2G; IPLA2-2; iPLA2gamma; PNPLA-gamma ). This is because many of the references cited (ref. #21, #22 and #24) relate to PLA2G6. 3. Patients with lymph node metastases are classified as stage III, while those with distant metastases, such as lung or liver metastases, are classified as stage IV. In addition, treatment and prognosis are very different between stage III and stage IV. Therefore, stage III and stage IV colorectal cancer patients should be distinguished as a separate group to study the impact of PNPLA8 expression. 4. Please describe the adjuvant and palliative chemotherapy received by the patients enrolled in this study.



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Reviewer's code:** 05330707

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Assistant Professor, Doctor

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-08-22

**Reviewer chosen by:** Ze-Mao Gong

**Reviewer accepted review:** 2023-12-20 21:56

**Reviewer performed review:** 2023-12-21 11:30

**Review time:** 13 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No





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#### **SPECIFIC COMMENTS TO AUTHORS**

All of my comments have been addressed. No further comments.