

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 66013

Title: Multiple subcellular localizations and functions of Protein kinase C δ in liver cancer

Reviewer's code: 03838204

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Japan

Manuscript submission date: 2021-03-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-03-26 08:28

Reviewer performed review: 2021-03-26 09:52

Review time: 1 Hour

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 Grade E: Do not publish
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



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SPECIFIC COMMENTS TO AUTHORS

The authors discussed the structural features of PKC δ and then focused on the functional diversity of PKC δ based on its subcellular localizations, such as the nucleus, cell surface, and extracellular space. These findings improved our knowledge of PKC δ involvement in liver cancer progression. Overall, it is a nice comprehensive review. I have several suggestions: 1. Most of the references were more than 10 years ago. The authors should try to summary the lasted developments. The more recent references should be added. 2. In Table 1. The relation between subcellular localizations and functions of PKC δ in liver cancer, the Function and Mechanisms were too simple. Please use a sentence rather than a word. 3. For STRUCTURAL FEATURES OF PKC δ , maybe the authors can add a protein structure figure to show its structure clearer. 4. For different section level, please use different font size or add section level numbers, such as format like 2.3. 5. In Figure 3, was it one cell? Was the line the cell membrane? It can be improved by adding more explanation words and colors.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 66013

Title: Multiple subcellular localizations and functions of Protein kinase C δ in liver cancer

Reviewer's code: 03656580

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Postdoc, Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Japan

Manuscript submission date: 2021-03-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-04-07 00:02

Reviewer performed review: 2021-04-07 00:23

Review time: 1 Hour

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
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



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SPECIFIC COMMENTS TO AUTHORS

PKC δ has been confirmed to play multifunctional roles in various cancers, including liver cancer. PKC δ has been shown to exert pleiotropic functions through various stimuli responsiveness, posttranslational modifications, and subcellular localization. PKC δ is secreted extracellularly and resides at the cell surface of liver cancer cells, which contributes to tumorigenesis. Authors summarized localization of cellular PKC δ and discussed its characteristic localization patterns and functions in liver cancer, and outline the involvement of PKC δ localized intra- and extracellularly with distinct functions in the progression of liver cancer. However, is PKC δ as a pivotal gene that affects the progression of liver cancer, or provide a new biological marker for the diagnosis and a molecular target for treatment of liver cancer in the future?

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 66013

Title: Multiple subcellular localizations and functions of protein kinase C δ in liver cancer

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03656580

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Postdoc, Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Japan

Manuscript submission date: 2021-03-26

Reviewer chosen by: Han Zhang (Online Science Editor)

Reviewer accepted review: 2021-09-17 05:49

Reviewer performed review: 2021-09-17 06:52

Review time: 1 Hour

Scientific quality	<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
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> <input checked="" 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
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

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

SPECIFIC COMMENTS TO AUTHORS

1. Authors found that PKC δ in the blood was elevated in liver cancer, had compared the ability of PKC δ to discriminate liver cancer with AFP and PIVKA-II, which are known biomarkers, and found PKC δ to be superior although the number of N is currently small. How to suggesting or confirmed that PKC δ may be a promising blood biomarker. Is this PKC δ level in blood or in liver tissues? or in AFP-NEGATIVE or lower level HCC? 2. Many studies have shown that PKC δ promotes the survival of multiple types of cancers, including non-small cell lung cancer, breast cancer, pancreatic cancer, chronic lymphocytic leukemia, and liver cancer. How about the PKC δ expression as a promising circulating marker for HCC?