**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology  
**Manuscript NO:** 66013  
**Title:** Multiple subcellular localizations and functions of Protein kinase Cδ 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

<table>
<thead>
<tr>
<th>Scientific quality</th>
<th>[ ] Grade A: Excellent</th>
<th>[ ] Grade B: Very good</th>
<th>[Y] Grade C: Good</th>
<th>[ ] Grade D: Fair</th>
<th>[ ] Grade E: Do not publish</th>
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<tbody>
<tr>
<td>Language quality</td>
<td>[ ] Grade A: Priority publishing</td>
<td>[Y] Grade B: Minor language polishing</td>
<td>[ ] Grade C: A great deal of language polishing</td>
<td>[ ] Grade D: Rejection</td>
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<td>Conclusion</td>
<td>[Y] Accept (High priority)</td>
<td>[ ] Accept (General priority)</td>
<td>[Y] Minor revision</td>
<td>[ ] Major revision</td>
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<td>Re-review</td>
<td>[Y] Yes</td>
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<td>Peer-reviewer</td>
<td>[Y] Anonymous</td>
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<td>statements</td>
<td>Conflicts-of-Interest: [ ] Yes</td>
<td>[Y] No</td>
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SPECIFIC COMMENTS TO AUTHORS

The authors discussed the structural features of PKCδ and then focused on the functional diversity of PKCδ based on its subcellular localizations, such as the nucleus, cell surface, and extracellular space. These findings improved our knowledge of PKCδ 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 PKCδ in liver cancer, the Function and Mechanisms were too simple. Please use a sentence rather than a word. 3. For STRUCTURAL FEATURES OF PKCδ, 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.
Name of journal: World Journal of Gastroenterology

Manuscript NO: 66013

Title: Multiple subcellular localizations and functions of Protein kinase Cδ 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 [ ] 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 [ ] Grade B: Minor language polishing [ Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection

Conclusion [ ] Accept (High priority) [ ] Accept (General priority) [ Y] Minor revision [ ] 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
PKCδ has been confirmed to play multifunctional roles in various cancers, including liver cancer. PKCδ has been shown to exert pleiotropic functions through various stimuli responsiveness, posttranslational modifications, and subcellular localization. PKCδ is secreted extracellularly and resides at the cell surface of liver cancer cells, which contributes to tumorigenesis. Authors summarized localization of cellular PKCδ and discussed its characteristic localization patterns and functions in liver cancer, and outline the involvement of PKCδ localized intra- and extracellularly with distinct functions in the progression of liver cancer. However, is PKCδ 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 Cδ 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
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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

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SPECIFIC COMMENTS TO AUTHORS

1. Authors found that PKCδ in the blood was elevated in liver cancer, had compared the ability of PKCδ to discriminate liver cancer with AFP and PIVKA-II, which are known biomarkers, and found PKCδ to be superior although the number of N is currently small. How to suggesting or confirmed that PKCδ may be a promising blood biomarker. Is this PKCδ level in blood or in liver tissues? or in AFP-NEGATIVE or lower level HCC?

2. Many studies have shown that PKCδ 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 PKCδ expression as a promising circulating marker for HCC?