

PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Oncology*

Manuscript NO: 85125

Title: Targeting KRAS in pancreatic adenocarcinoma: Progress in demystifying the holy grail

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05848410

Position: Peer Reviewer

Academic degree: Doctor, MMed, PhD

Professional title: Chief Doctor, Chief Physician, Dean, Doctor, Professor, Surgeon

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2023-04-12

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-04-18 08:27

Reviewer performed review: 2023-04-22 14:07

Review time: 4 Days and 5 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 Grade E: Do not publish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 type="checkbox"/> Grade B: Good <input checked="" 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 type="checkbox"/> Grade B: Good <input checked="" 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 checked="" type="checkbox"/> Accept (General priority) <input 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 type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors discussed the KRAS and its pathway from basic research to clinical trials. The pathway including KRAS, MEK, ERK, PI3K, and so on has been studied a lot and the drugs targeted the pathway also been studied a lot, so now there are many ongoing clinical trials. Since it is a mini-review, it is fair that the authors only placed the full informations but not discussed a lot, therefore, this manuscript does not have enough novelty. And finally, the most important issue is who is going to be the audience of this manuscript.

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Title: Targeting KRAS in pancreatic adenocarcinoma: Progress in demystifying the holy grail

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03765475

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: United States

Manuscript submission date: 2023-04-12

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-06-15 16:35

Reviewer performed review: 2023-06-15 16:45

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
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
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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="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is an excellent mini-review on a hot-topic in pancreatic pathology. The review is timely and well-written, with excellent tables too. The figures are very clear. Here some minor suggestions to improve this paper: 1) the readers should understand why KRAS-mutated pancreatic cancer is totally different from KRAS wild type. Please add some sentences in the Introduction section regarding the peculiarities of KRAS-wt pancreatic cancer. 2) please add some specific sentences regarding KRAS G12C (and related drugs, too) as a promising target in lung cancer patients (KRAS paragraph). Otherwise, excellent mini-review.

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Title: Targeting KRAS in pancreatic adenocarcinoma: Progress in demystifying the holy grail

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05469117

Position: Editorial Board

Academic degree: PhD

Professional title: Adjunct Professor, Chief Physician, Deputy Director

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2023-04-12

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-06-18 17:17

Reviewer performed review: 2023-06-20 17:22

Review time: 2 Days

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
Novelty of 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 novelty
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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

Thank you very much for inviting me to evaluate the mini reviews titled “Targeting KRAS in Pancreatic Adenocarcinoma - Progress in Demystifying the Holy Grail”. In this article the authors summarized some of the efforts made to target the KRAS pathway which plays an important role in cancer cell proliferation, differentiation, metabolism, and survival, making it an essential mutation for targeted therapy in PC , discuss the challenges, and shed light on promising clinical trials. The information in this review may be useful to clinical communities. The paper is well arranged and the logic is clear, and the provided figure and tables are well composed and understandable. The quality of language of the manuscript is quite acceptable for me. But this article has “obvious differences”: 1) Viewpoints involved in the article lacks a comprehensive discussion, and directly uses examples for discussion. 2) The treatment methods mentioned explain the mechanisms, but do not give specific efficacy data, which is puzzling. So, I recommend that this manuscript may be accepted after major revision. Here is a question for the authors, Please systematically explain how KRAS mutations drive tumor progression and possible drug resistance mechanisms, which is an important part

of the discussion on this topic?

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Peer-review model: Single blind

Reviewer's code: 05469117

Position: Editorial Board

Academic degree: PhD

Professional title: Adjunct Professor, Chief Physician, Deputy Director

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2023-04-12

Reviewer chosen by: Cong Lin

Reviewer accepted review: 2023-07-07 15:02

Reviewer performed review: 2023-07-07 15:51

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 [Y] No

SPECIFIC COMMENTS TO AUTHORS

The revised article can be accepted for publication