

Editor, World Journal of Gastroenterology,

Dear Dr. Chuan-Zhao Zhang,

Please find below our manuscript entitled "Therapeutic Resistance in PDAC: Current Challenges and Future Opportunities" (ID65602), which we wish to be considered for publication as a review article in the World Journal of Gastroenterology. We would like to thank the reviewers for their suggestions to improve the manuscript. Please find below our point-by-point response to all the reviewer's concerns, and we strongly believe that the manuscript in its revised version appropriately fits into your journal. We have also responded to some of the issues raised by the science editor.

All authors have reviewed the manuscript and have no conflict of interest to declare.

We thank you for considering our manuscript for publication.

Best Regards,

Vikas Bhardwaj

Jefferson College of Pharmacy,

Jefferson University,

901 Walnut Street, 910, Philadelphia, PA 19107

Reviewer 1:

"Therapeutic Resistance in PDAC: Current Challenges and Future Opportunities" by Jain and Bhardwaj is an excellent review on the underlying causes of therapeutic resistance in PDAC and clinical trials trying to circumvent this resistance. It is very well organized and written and will help young and experienced researchers and clinicians orient themselves in this complex terrain.

We would like to thank the reviewer for a thorough review of the manuscript.

Reviewer 2:

The prognosis of pancreatic cancer is very poor, chemotherapy is an important treatment, drug resistance is a problem that doctors often encounter. This is a very detailed overview, rich in content, clear. I highly appreciate the author's detailed literature review, but the length of the article is too long to be published in journals, and it is more suitable to be published as a book after expansion. If the author wants to publish this article in the journal, please reduce the length as much as possible.

We would like to thank the reviewer for a thorough review of the manuscript. We have significantly reduced the length of the manuscript, however, have made sure that the important aspects covered in the manuscript are not lost.

Science editor:

1 Scientific quality: The manuscript describes a review of the therapeutic resistance in PDAC. The topic is within the scope of the WJG.

- (1) Classification: Grade B and Grade A;
- (2) Summary of the Peer-Review Report: This is a very detailed overview, rich in content, clear. It is very well organized and written and will help young and experienced researchers and clinicians orient themselves in this complex terrain. However, the manuscript is longer. The questions raised by the reviewers should be answered;
- (3) Format: There are 2 tables;
- (4) References: A total of 273 references are cited, including 52 references published in the last 3 years; and
- (5) Self-cited references: There is no self-cited reference.

2 Language evaluation: Classification: Grade B and Grade A.

3 Academic norms and rules: The authors need to provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. No academic misconduct was found in the

Bing search. We have provided the conflict of interest disclosure form and copyright license agreement

4 Supplementary comments: This is an invited manuscript. The topic has not previously been published in the WJG.

5 Issues raised:

(1) I found no “Author contribution” section. Please provide the author contributions; **We have added “author contribution” section**

(2) I found no “Core tip” section. Please add; **We have added “Core tip” section**

(3) I found no “Key Words” section. Please add; and **We have added “Key words” section**

(4) I found the authors did not add the PMID and DOI in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. **The references have been updated to show PMID and DOI**
Please revise throughout.

6 Recommendation: Conditionally accepted.