

Dear Editor and Reviewers

Thank you for your time to review this manuscript. We sincerely appreciate the feedback. We have carefully amended the manuscript accordingly. Please find our point-to-point response to the comments. We appreciate your favorable response to our action. Thank you!

Comments from Reviewer 1 (00077376)

1. *Immunotherapy has been raised as a breakthrough of cancer therapy, which warrants further exploration for PDAC treatment. However, immunotherapy for PDAC is largely limited by its immune evasion barrier. This review is well written for helping us to understand the diverse mechanisms underlying the immune evasion in PDAC, focusing on targeting histone deacetylase (HDAC) as a strategy to reverse immune evasion in PDAC. The following is the minor comment to this review. # Figures 1, 2 and 3 seem to be originally drawn by the authors; however, the concept is based on the results of previous studies. Therefore, it is recommended that several references should be cited like “This figure is an original creation based on these references“.*

Response to Reviewer 1

Thank you for the comment. We have added the following line in the respective figures.

- “This figure is an original creation based on references [8-14].” in figure legend for figure 1.
- “This figure is an original creation based on reference [20]” in figure legend for figure 2.
- “This figure is an original creation based on references [6] and [72].” in figure legend for figure 3.

Comments from Reviewer 2 (04876783)

1. *The review of Sim W and co-workers, discusses current state of the art in pancreatic cancer treatment progress form the level of immune response and histone deacetylase inhibitors (HDACi) potential. The paper is very interesting and contains a number of valuable information briefly summarizing achievements and failures of the ongoing anticancer treatment in pancreatic cancer that take advantage of the HDACi. - The content of the article well matches to the profile of the journal, and quite well meets the formula of the review paper. - The introduction is coherent and very well bring s to the topic of the paper. - Included table and figures well illustrate ethos of the review, summarize the data and increase the quality and clarity of the paper. - The references are properly chosen. Comments: - The effect of HDACi on angiogenesis is minimally mentioned and despite of the non-specific effect should be developed.*

Response to Reviewer 2

Thank you for the comment. We have added a paragraph regarding HDAC inhibitor in angiogenesis under “HDAC INHIBITORS AS CANCER THERAPY” in the manuscript.

2. *Also the mRNA vaccines for pancreatic cancer are not indicated at least against KRAS mutations, as the authors describe the genetic background of the disease. –*

Response to Reviewer 2

Thank you for the comment. We have added a paragraph about mRNA vaccine in pancreatic cancer and elaborated the possible of its combination with HDAC inhibitor under “HDAC inhibitors enhance tumor immunogenicity” in the manuscript.

3. *Some typing errors should be removed before publication, e.g. in abstract “We review the evidence on HDAC inhibitors in tumor eradication “tumor”?.....*

Response to Reviewer 2

Thank you for the comment. We have amended those typing errors.

4. *Sometimes histone deacetylase is in singular and should be in plural, please put an attention and check, also regarding abbreviation. I do recommend the publication of the paper in the World Journal of Gastroenterology after minor revision.*

Response to Reviewer 2

Thank you for the comment. We have amended those typing errors.

Comments from Science Editor

1. *The author in this Review article described current state of the art in pancreatic cancer treatment progress from the level of immune response and histone deacetylase inhibitors potential. The Abbreviations section and running title are missing.*

Response to Science Editor

Thank you for the comment. We added abbreviation section before reference list. The running title is placed right after the title of the manuscript.

2. *The number of references published in the last 5 years isn't appropriate. However, according the reviewer suggestions, it is appropriate for publication on WJG.*
Language Quality: Grade B (Minor language polishing)
Scientific Quality: Grade B (Very good)

Response to Science Editor

Thank you for the comment. We have replaced those papers published more than 5 years ago whenever possible. However, many of those papers are the first paper published on the cited concept or findings. Thus, we feel it is appropriate to keep these references in the review to ensure the original ideal/concept cited in the review can be acknowledged accordingly.

Comments from Company Editor-in-Chief

1. *I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content. In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author; and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and copyrights. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022. If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For example, "Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. World J Gastroenterol 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]". And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable.*

Response to Science Editor

Thank you for the comment. We have prepared the figures and tables according to the suggestion.