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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 63433

Title: Modulation of cell physiology under hypoxia in pancreatic cancer

Reviewer's code: 03004124
Position: Editorial Board
Academic degree: MD
Professional title: Research Assistant Professor
Reviewer's Country/Territory: Italy
Author's Country/Territory: Spain

Manuscript submission date: 2021-01-28
Reviewer chosen by: Jin-Lei Wang
Reviewer accepted review: 2021-04-01 22:30
Reviewer performed review: 2021-04-02 14:13
Review time: 15 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] 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: [ ] Anonymous [Y] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

I have read with great interest and enthusiasm this review article. Authors present an extensive overview about role and mechanisms related to hypoxia in pancreatic cancer. They show all the relationships between hypoxic environment and other factors involved in pancreatic cancer. The major point of interest of this paper is represented by the interactions between hypoxia and tumor microenvironment components; in fact they play a crucial role in pancreatic cancer progression and resistance to current treatments. The manuscript is well written and clear. I only suggest to improve the manuscript adding some datas about potential treatments directed against hypoxia (i.e. evofosfamide), underlining how and why these agents have failed to demonstrate survival benefit in pancreatic cancer therapy up to date. As for the references, I just to advise to consider the citation of the paper published by Parente P. et al in 2019 in Gastroenterology Research and Practice (Crosstalk between the tumor microenvironment and immune-system in Pancreatic Ductal Adenocarcinoma: potential targets for therapeutic approaches). Based on these considerations, I recommend the paper for publication after improving it with these minor revisions.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 63433

Title: Modulation of cell physiology under hypoxia in pancreatic cancer

Reviewer's code: 05199120
Position: Peer Reviewer
Academic degree: MD
Professional title: Associate Chief Physician
Reviewer's Country/Territory: China
Author's Country/Territory: Spain

Manuscript submission date: 2021-01-28
Reviewer chosen by: Jin-Lei Wang
Reviewer accepted review: 2021-03-31 15:06
Reviewer performed review: 2021-04-08 01:41
Review time: 7 Days and 10 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] 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

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SPECIFIC COMMENTS TO AUTHORS

The proliferation of pancreatic tumor cells is often accompanied by the underdevelopment of blood microcirculation, and hypoxia leads to the activation of different intracellular pathways and alterations in cellular energy metabolism, all of which are in turn regulated by hypoxia. This paper focuses on the latest research progress on how pancreatic tumor cells adapt to hypoxia, with a novel idea, abundant content, clear arguments and sufficient arguments, but as a whole, there are some problems: 1. some contents in the paper are not marked with references. 2. There are more cytokines involved in hypoxia and MAPKs signaling in pancreatic cancer, and it is suggested to provide a vivid schematic diagram to show more intuitive. 3. The role of ERK5 in the development of pancreatic cancer in the main text is suggested to be further explained. 4. Figures 1, 2, 3 and 4 are not labeled properly, and legends should be provided.