



PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 39167

Title: Shattering the castle walls: Anti-stromal therapy for pancreatic cancer

Reviewer's code: 02954661

Reviewer's country: Romania

Science editor: Li-Jun Cui

Date sent for review: 2018-03-30

Date reviewed: 2018-03-31

Review time: 1 Day

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Dear Editor, Thank you for the opportunity to review the interesting manuscript entitled 'Shattering the castle walls: Anti-stromal therapy for pancreatic cancer'. The authors reviewed the role of pancreatic cancer - peritumoral stroma interaction, and the therapeutic possibilities to increase the cytotoxic effects of current chemotherapy



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regimen targeting also peritumoral stroma. The paper has merits to be accepted after minor revision. Major concerns: - I suggest a table in which should be done a synthesis of the review; I suggest as columns: headings from the article, therapeutic strategies, current existing studies, etc. Minor concerns: In keywords: SPARC - please detail what means this abbreviation. In figure 1 - please detail all abbreviations. I recommend to authors our meta-analysis: 'Negoi I, Hostiuc S, Sartelli M, Negoi RI, Beuran M. MicroRNA-21 as a prognostic biomarker in patients with pancreatic cancer-A systematic review and meta-analysis. The American Journal of Surgery. 2017 Sep 1;214(3):515-24'. We found that 'The microRNA-21 upregulation was significantly associated with poorer overall survival, disease-free survival, and progression-free survival. The subgroup analysis revealed that microRNA-21 overexpression has a significant higher prognostic value for patients who receive adjuvant chemotherapy. Increased microRNA-21 was associated with a statistically significant higher rate of metastatic lymph nodes and poorly differentiated tumors.

INITIAL REVIEW OF THE MANUSCRIPT

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[Y] No



PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 39167

Title: Shattering the castle walls: Anti-stromal therapy for pancreatic cancer

Reviewer's code: 03472014

Reviewer's country: Malaysia

Science editor: Li-Jun Cui

Date sent for review: 2018-03-30

Date reviewed: 2018-04-01

Review time: 2 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The minireview by Ozkan Kanat and Hulya Ertas highlights role of stroma in the development and progression of pancreatic cancer (PC) and summarises the current status of anti-stromal therapies in the management of metastatic PC. The topic is of significant facet in the development of effective cancer therapy. This manuscript can



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be scholarly presented by having the following revision; 1. Research findings and literature on exosome-mediated PC progression by Pancreatic Stellate/Stroma Cells need to be reviewed. It is suggested to have these literatures presented to support the imperative role of stroma in cancer progression. 2. It has been shown that PSCs/Stoma plays crucial role in formation cancer stem cells (CSCs) which confers aggressiveness/invasiveness in tumour, hence a section on the mechanism of CSC induction and regulation by stoma will be intriguingly develop the discussion and knowledge around this topic. 3. Section on "Upregulation of microRNAs in PSCs": It is not clear on why the section focused on only miR-21. Is this the only microRNA implicated/upregulated? A comprehensive microRNAs list and mechanism implicated in this process will enhance the discussion. 4. It is suggested to provide a critical discussion on challenges and future perspectives as a section.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 39167

Title: Shattering the castle walls: Anti-stromal therapy for pancreatic cancer

Reviewer's code: 03471272

Reviewer's country: Japan

Science editor: Li-Jun Cui

Date sent for review: 2018-03-30

Date reviewed: 2018-04-03

Review time: 4 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
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publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The review provided useful information related to anti-stromal therapy for pancreatic cancer. The manuscript would improve if the authors summarize pros and cons of stroma-targeting therapy. In addition, some points need to be added or revised before this paper can be considered for publication. 1. The authors should provide their own



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data. 2. It would be better to discuss other components of stroma (vessels, immune cells, etc). 3. The authors described "PSCs resemble myofibroblasts"; therefore, it would be better to discuss difference between those cells. 4. It would be better to discuss the side effects of stroma-targeting therapy.

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