



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 42308

Title: Molecular detection of epithelial-mesenchymal transition markers in circulating tumor cells from pancreatic cancer patients: Potential role in clinical practice

Reviewer's code: 00504383

Reviewer's country: Lebanon

Science editor: Ruo-Yu Ma

Date sent for review: 2018-10-15

Date reviewed: 2018-10-19

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 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 checked="" 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 checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

In this manuscript, the authors evaluated the EMT transition of circulating tumor cells (CTC) and the clinical properties of these EMT-CTC subpopulations in patients with pancreatic ductal adenocarcinoma. This study suffers from a small sample size. It was



performed despite the known disconnect between EMT and metastasis in pancreatic cancer (Martin C. Whittle, Sunil R. Hingorani, Oncotarget 2015), a paper that the authors do not cite. The implications of this disconnect in light of the current findings should be presented and discussed. This paper presents interesting findings on 80 patients who were enrolled in the study for CTC evaluation of epithelial cell marker CK or EpCAM(E-CTC), the mesenchymal cell marker vimentin and Twist (M-CTC), or both. The main finding is that CTCs are associated with the pathological features in pancreatic cancer patients and thus could be novel prognostic factors for the disease. The main problem with this paper is that it includes many abbreviations and English syntax errors to an extent that such abbreviations/weak statements hinder the understanding of paragraphs. The interpretation of some of the results are difficult because of their poor presentation. Some comments that could help authors to improve the paper before resubmission are listed below: 1. The general information on human subjects and the correlation of total CTC status with clinicopathological factors (Table 2) could be made more detailed (for example it would be interesting to show mean age, median age, ethnic group) 2. On page 11/26 last line of paragraph of Results, it is not clear where the numbers 67.5%, 42.5%, 32.5% are derived. Data should be presented more clearly in Table 1 to align with text. 3. Table 1 and Figure 1 should be combined 4. Table 3 results are not mentioned in text nor are data in this table discussed. This is also the case for figures 3D and 3F 5. For ease of understanding the results, it is better to have different labels on the y-axis of figure 2E and F to reflect overall survival and progression free survival respectively (rather than just mention it in legend) 6. In figure 2G, the CTC negative and positive lymphocytes results appear to be overlapping yet they are statistically significant? 7. delete all empty pages in the manuscript 8. Tables 4-1 and 4-3 are the same! 9. Figures 2 and 3 labels, what is AJCC stages? What is CTM on page 19? CK20 on page 16? Etc.. 10. Improve write up of paper, have a native English speaker



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7901 Stoneridge Drive, Suite 501,
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check it for errors and define all abbreviations upon first use. Even abstract has too many abbreviations!

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 42308

Title: Molecular detection of epithelial-mesenchymal transition markers in circulating tumor cells from pancreatic cancer patients: Potential role in clinical practice

Reviewer's code: 00505755

Reviewer's country: Japan

Science editor: Ruo-Yu Ma

Date sent for review: 2018-10-31

Date reviewed: 2018-10-31

Review time: 3 Hours

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 polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer's expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Minor revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is a very interesting study about circulating tumor cells that have a property as the prognostic indicator. The background and introduction describing that CTCs have a property as prognostic indicator may be revised to include the detailed information



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about the interaction between CTCs and PDAC. Please check abbreviations carefully.
Proofreading is needed.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 42308

Title: Molecular detection of epithelial-mesenchymal transition markers in circulating tumor cells from pancreatic cancer patients: Potential role in clinical practice

Reviewer’s code: 02441100

Reviewer’s country: Italy

Science editor: Ruo-Yu Ma

Date sent for review: 2018-10-15

Date reviewed: 2018-11-01

Review time: 17 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 checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer’s expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Minor revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is an interesting study on an intriguing phenomenon in tumor progression, that is the epithelial-mesenchymal transition . The title reflects the main topic of the text. The abstract is fully inclusive of the described concepts of the manuscript. Key words



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reflect the focus of the manuscript except for the word “ macrophages” The text is well written; the content is original; statistical analysis is appropriate. Results are adequately reported and representative of the objectives of the study. The “Discussion” section is well-developed ; figures and tables are appropriately illustrative of the study. The references are updated. However several points should be checked: 1) In “Introduction” (page 5) the sentence “...(EUS-FNA) is the current gold standard technique” should be clarified. 2) “epithelia-to-mesenchymal transition (EMT)” (pages 6-7) is internationally named “epithelial- mesenchymal transistion” 3) “preoperative chemotherapy “ (page 8) should be checked 4) In “Results- Correlation of CTCs with clinicopathological feature (page12) “(Tab. 3)” should be added at the end of the sentence “Multivariate analysis revealed that ...for overall survival in patients with PDAC. Moreover “ (Figure 2F and G)” on page 13 should be changed to “(Figure 2G and H)” according to the legend of Figure 2. 5) In “Results- Association between CTC- EMT subpopulation and clinicopathological features” is reported that “ The presence of E-CTCs was positively correlated with TMN stage($P\leq 0,01$) and distant metastasis ($P\leq 0,01$).” However in Table 4 distant metastasis is not indicated as clinicopathological factor (pay attention: Table 4.3 is analogous to Table 4.1!!) 6) The acronym CTMs in “Discussion” (Pag.20) should be defined 7) At last the legend of table 1 should be checked : why “ total and vim+ CTC status”? Vim+ is not included in “total CTCs status”?

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7901 Stoneridge Drive, Suite 501,
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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 42308

Title: Molecular detection of epithelial-mesenchymal transition markers in circulating tumor cells from pancreatic cancer patients: Potential role in clinical practice

Reviewer's code: 00070509

Reviewer's country: South Korea

Science editor: Ruo-Yu Ma

Date sent for review: 2018-10-31

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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
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<input 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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			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
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SPECIFIC COMMENTS TO AUTHORS

The authors hypothesize that both total CTC number and CTC EMT phenotype may act as potential biomarkers for PDAC prognosis. They conclude that CTCs are highly associated with PDAC clinicopathological features and are a novel prognostic factor for



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this disease through their experiments. The paper is well written. Conclusions drawn from the experiments are adequate. I suggest the acceptance of the paper without further changes. However, there is one thing to be corrected in Figure 1. (B) Biophenotypic epithelial/mesenchymal CTCs. --> Mesenchymal CTCs. (C) Mesenchymal CTCs. --> Biophenotypic epithelial/mesenchymal CTCs.

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