

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 24264

Title: Epithelial-to-mesenchymal transition in pancreatic ductal adenocarcinoma: characterization in a 3D-cell culture model

Reviewer's code: 00227509

Reviewer's country: Japan

Science editor: Ya-Juan Ma

Date sent for review: 2016-01-21 16:49

Date reviewed: 2016-01-27 11:17

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This manuscript describes EMT phenomena in 3-D cell culture, using 3 kinds of pancreatic cancer cell lines. The authors investigated ultrastructural characterization of EMT with transmission electron microscopy and expression of EMT-associated protein such as α SMA and E-cadherin. A marked EMT phenomenon was observed in 3-D cell culture, compared to 2-D culture. The results are very interesting. The authors should change a few points before publication as described below. 1. The authors should describe phenotype of 3 pancreatic cancer cell lines and discuss the relationship between EMT potentials and character of each cell. 2. Conclusion is too long. The authors should make the conclusion shorter.

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Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 24264

Title: Epithelial-to-mesenchymal transition in pancreatic ductal adenocarcinoma: characterization in a 3D-cell culture model

Reviewer's code: 02439200

Reviewer's country: United States

Science editor: Ya-Juan Ma

Date sent for review: 2016-01-21 16:49

Date reviewed: 2016-01-28 23:17

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

The manuscript entitled "Epithelial-to-mesenchymal transition in pancreatic ductal adenocarcinoma" addresses an important aspect of tumorigenesis, namely EMT. Although this is an important area of investigation with potential applications to the development and progression of PDAC, I have some significant concerns about this manuscript. Major concerns: 1) The authors state that E-cadherin is down regulated in PDAC yet they show that the expression of E-cadherin is increased in 3-D cultures. 2) Additionally, the authors state that in 3-D cultures cells undergoing EMT dedifferentiate. Although some cells in 3-D cultures express α -SMA and Col-1, so do some cells in the 2-D cultures. These proteins are normally markers for activated pancreatic stellate cells. Are they expressed in metastatic PDAC cells? 3) It is not clear what the overall utility of 3-D culturing of PDAC cells is. There is tremendous variation within and between the various cell lines. It should be clearly pointed out how this study will facilitate investigation of PDAC initiation and progression. Minor concerns: 1) In general the micrographs are not large enough or of high enough quality to assess the validity of the authors interpretation of the micrographs. 2) The authors continually interpret the micrographs



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regarding subcellular structures and organelles but do not provide evidence that these structures and organelles are in fact what the authors believe they are. Additionally, the magnification does not always seem to be right. The nuclei under similar conditions are not the same size. 3) The data presented in this manuscript would be much stronger if the co-localization of the various proteins was investigated. 4) The 2-D cultures are shown in longitudinal sections whereas the 3-D cultures are shown in vertical cross-sections. It is impossible to compare these images to each other. How long have these cells been culture before fixation. 5) In figure 8 it is unclear what bands are being quantified. Are the authors referring to all bands or just the 120 kD band? 6) This manuscript is full of jargon and needs to be carefully proofread.

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Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 24264

Title: Epithelial-to-mesenchymal transition in pancreatic ductal adenocarcinoma: characterization in a 3D-cell culture model

Reviewer's code: 02543990

Reviewer's country: United States

Science editor: Ya-Juan Ma

Date sent for review: 2016-01-21 16:49

Date reviewed: 2016-01-29 05:17

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
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		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This is an interesting study that investigated the cellular features of and EMT related marker expression in pancreatic cancer cell lines under 2D and 3D culture conditions. The experiments are well designed and very nice images are provided. However, there are still a few issues need to be addressed to improve the quality of this manuscript. 1. Statistical results should be presented in Figures 8A, 8B, and 8D. 2. For the cell line of HPAC, the expression of E-cadherin at mRNA level (Figure 8A) doesn't agree with the protein level (Figure 8B & 8C), what is the potential mechanisms behind? 3. Compared to 2D culture condition, cells cultured in 3D condition tended to express similar or reduced level of α SMA in both HPAF-II and HPAC cell lines, but it was drastically opposite in PL45 cells, how to explain it?