

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23832

Title: The Metabolic Phenotype of Pancreatic Cancer.

Reviewer's code: 00227505

Reviewer's country: Japan

Science editor: Ya-Juan Ma

Date sent for review: 2015-12-22 09:40

Date reviewed: 2016-01-04 16:40

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" 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 checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The manuscript titled "The Metabolic Phenotype of Pancreatic Cancer" has been reviewed. This manuscript is well investigated and well written. However, I recommend to make some amendment to the manuscript Critique: 1. The authors found that there was consistent over-expression of glycolytic enzymes and lactate dehydrogenase in keeping with the Warburg effect to facilitate rapid ATP production from glycolysis. Do the authors have any data to show the results? If so, it strengthens the manuscript. 2. The authors state "Further characterisation of the PDAC metabolic phenotype is necessary as currently there are few clinical studies and no successful clinical trials targeting metabolic enzymes." Do the authors have any plan to conduct the clinical trial? 3. In the section of conclusion, the authors referred to the article from Ko et al. I realized the authors quoted the article since none of the article regarding pancreatic article is published. But the character between HCC and PDAC is completely different. The sentences would be needed to rewrite. The sentences would be needed to change or rewrite.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23832

Title: The Metabolic Phenotype of Pancreatic Cancer.

Reviewer's code: 00074342

Reviewer's country: Finland

Science editor: Ya-Juan Ma

Date sent for review: 2015-12-22 09:40

Date reviewed: 2016-01-07 14:32

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

COMMENTS TO AUTHORS

I found this manuscript a pleasure to read. The subject was interesting, details presented systematically. If I understood right, metabolic phenotype was mainly studied in cell lines. It would be very interesting to test those in real patient cohorts. Tables: could you please add the abbreviations in the table? It would make the article easier to read.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23832

Title: The Metabolic Phenotype of Pancreatic Cancer.

Reviewer's code: 01557283

Reviewer's country: Japan

Science editor: Ya-Juan Ma

Date sent for review: 2015-12-22 09:40

Date reviewed: 2016-01-09 06:59

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" 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"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input checked="" 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

The present systematic review of the literatures focuses on glycolytic and mitochondrial oxidative phosphorylation enzymes of PDAC, and is interesting to consider one of the therapeutic options for PDAC. However, the authors should show why the present review is very attractive, and show a strong conclusion. Some major comments are listed as described below. Abstract. In the results section, the authors did not state any concrete results. The authors should express some main concrete findings and targets to treat PDAC. Introduction. The authors should clearly state how important reviewing tumor-related metabolic enzyme is. Results. The authors should simplify results. The results section is too long. Conclusion. The authors should state what target could be very attractive to treat PDAC. Tables. There are many words in the tables. The authors should make an effort to simplify them, e.g., Table 1 & 3.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23832

Title: The Metabolic Phenotype of Pancreatic Cancer.

Reviewer's code: 01212501

Reviewer's country: South Korea

Science editor: Ya-Juan Ma

Date sent for review: 2015-12-22 09:40

Date reviewed: 2016-01-11 07:12

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" 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 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 type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" 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 checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

1. Authors did a great job to summarize the metabolic phenotype of PDAC. It would be better that authors could suggest the differences between PDAC and other cancer in terms of metabolic phenotype. Even though author commented on "metabolic phenotype" of pancreatic cancer, these metabolic alterations may be similar to those of other cancers. 2. Adding appropriate figures showing metabolic characteristics of pancreatic cancer will be more helpful for readers. 3. In oncologic practice of pancreatic cancer, there are, by and large, two clinical phenotype of metabolism of pancreatic cancer. One is high FDG-uptake pancreatic cancer and another is low FDG-uptake pancreatic cancer. Can authors suggest the underlying oncologic meaning based on these review knowledge? 4. Authors suggested that metabolic phenotype could be potential target in treating pancreatic cancer. On the other hand, it would be more helpful to explain the current obstacles, such as drug specific toxicity to cancer; how can metabolite-targeted drug differentiate patient's normal enzyme from cancers' ones? 5. Future perspective sessions need to be separated from conclusion sessions. 6. MCT-4 session need to be added in discussing metabolic phenotype of cancers. 7. Also, other metabolites, such as AA, Lipid.. or authors need to modify the title as " The glucose



BAISHIDENG PUBLISHING GROUP INC

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

<http://www.wjgnet.com>

metabolic phenotype of pancreatic cancer".

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23832

Title: The Metabolic Phenotype of Pancreatic Cancer.

Reviewer's code: 00069894

Reviewer's country: China

Science editor: Ya-Juan Ma

Date sent for review: 2015-12-22 09:40

Date reviewed: 2016-01-11 13:16

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" 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"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
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<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The authors reviewed quite a amount of literatures to illustrate glycolytic and MOP enzymes in PDAC. I can tell the authors endeavor to this heavy and well designed work. In addition, the language was clear, accurate and professional. My personal opinions are as following: 1.The title 'The Metabolic Phenotype of Pancreatic Cancer' was way too common and failed to highlight the significance of the research in details. The authors tried to summary the enzymes involved in PDAC from a microscopic view, the subject of this paper should be more specific. Besides, my group has already published a paper regarding 'Metabolic Phenotypes in Pancreatic Cancer' in PLOS ONE [1] and I believe some of the research were overlapped. As a result, it is highly recommend that the authors revise the subject. 2.The metabolic types of cancer were extremely complicated and a well-accepted conclusion was far to draw. The metabolic phenotypes of tumors were roughly classified into two categories, glucose- and glutamine-dependent metabolism. There were Warburg type, reverse Warburg type, mixed type, and null type in glucose-dependent metabolism, and canonical type, non-canonical type, mixed type, null type in glutamine-dependent metabolism. What are the authors' viewpoints referring to the relationship among the various metabolic types? In the

manuscript, why would the researches simply concentrate on Warburg effect irrespective of the remaining mentioned above? 3.The metabolic enzymes in PDAC were demonstrated in cell lines. Do the authors tend to interpret the conundrum in tissues or even patients in the future? 4.To me, the RESULTS was too lengthy and difficult to understand. For general readers, it would be better if the professional interpretation were concise. As for the CONCLUSION, the authors did not give a concrete summing-up and failed to underline the significance of the research. In some point, the abundant summary came to nothing. In what way can the research benefit the clinical application in the future? [1] Yu M, Zhou Q, Zhou Y, Fu Z, Tan L, Ye X, et al. (2015) Metabolic Phenotypes in Pancreatic Cancer. PLoS ONE 10(2): e0115153. doi:10.1371/journal.pone.0115153