



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 48768

**Title:** Integrative analysis of the inverse expression patterns in pancreas development and cancer progression

**Reviewer’s code:** 02845261

**Reviewer’s country:** Greece

**Science editor:** Jia-Ping Yan

**Reviewer accepted review:** 2019-05-06 19:42

**Reviewer performed review:** 2019-05-10 10:19

**Review time:** 3 Days and 14 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	(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 checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

Critique -This paper represents a basic study regarding the inverse gene expression patterns in pancreas development and pancreatic cancer progression. The authors studied 6 pancreatic cancer datasets collected form TCGA database to establish



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differentially expressed genes related to pancreas development and pancreatic cancer. Further, gene clusters with highly similar interpretation patterns between pancreas development and pancreatic cancer progression were established by SOM-SVD. The matrices with 1,257 genes, which obtained from this analysis, were clustered into four gene clusters. The cluster 2 and cluster 4 were highly expressed at the early stage, while they were identified as the continuously up-regulated expression patterns. In contrast, low gene interpretation was observed in cluster 1 and cluster 3 at the early stage and increased with time. So, they were identified as continuously down-regulated expression patterns. The whole idea seems very smart and indeed it is reasonable that during the pancreatic cancer developmental process, the same groups of genes which control the embryonic development of normal pancreas, probably interact, in a mutated status, and generate the abnormal proliferation of malignant cells. -However, there are several recent papers referring to pancreatic cancer genetics, such as: Cicens J, et al. *Cancers* 2017, 9, 42; doi:10.3390/cancers9050042, Knudsen ES, et al. *Gut* 2018;67:508–520, The Cancer Genome Atlas Research Network *Cancer Cell* 32, 185–203, August 14, 2017, and several other important papers in that topic, analyzing the various genomic characteristics of pancreatic cancer. The authors should refer to these recent papers in their Discussion and try to find relations with them. -The authors state that glycerophospholipid metabolism pathway plays an important role in pancreatic cancer tumorigenesis. The authors should add a comment analyzing the importance of this pathway, and probably the relative importance of the 3 or 4 most important pathways presented in Table 2. -The Core Tip of the paper should be minimized, whereas the Discussion should be enriched. -The whole paper should be seen and corrected. by an expert in English language and terminology.

**INITIAL REVIEW OF THE MANUSCRIPT**



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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 48768

**Title:** Integrative analysis of the inverse expression patterns in pancreas development and cancer progression

**Reviewer's code:** 03545890

**Reviewer's country:** Greece

**Science editor:** Jia-Ping Yan

**Reviewer accepted review:** 2019-05-07 03:21

**Reviewer performed review:** 2019-05-12 16:22

**Review time:** 5 Days and 13 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 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**

There are not specific comments to the authors as this is an investigated study based on the analysis of genes which are involved in the metabolic pathway of pancreas. Perhaps on limitation is related to the small number of pancreatic samples



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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 48768

**Title:** Integrative analysis of the inverse expression patterns in pancreas development and cancer progression

**Reviewer's code:** 02445886

**Reviewer's country:** Russia

**Science editor:** Jia-Ping Yan

**Reviewer accepted review:** 2019-05-05 10:48

**Reviewer performed review:** 2019-05-16 13:56

**Review time:** 11 Days and 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 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 checked="" 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 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 paper discusses molecular interpretation patterns of pancreas development and cancer progression. The title is in accordance with the main subject/hypothesis of the manuscript, and the abstract and the key words reflect the main results of the article. The



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manuscript clearly explains methods in adequate detail. The statistical analysis in this paper is suitable for the goals of this study. The results show continuously dysregulated interpretation patterns in pancreas development and pancreatic cancer. The data obtained is discussed well, recent papers in this field are cited. The results obtained will be useful in the larger-scale development and integrative cancer analysis. The figures are appropriately illustrative of the paper contents, but the legends do not explain drawings in sufficient detail. The manuscript is well written but needs minor language polishing. I suggest to accept the manuscript with minor revisions.

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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 48768

**Title:** Integrative analysis of the inverse expression patterns in pancreas development and cancer progression

**Reviewer's code:** 02922607

**Reviewer's country:** Pakistan

**Science editor:** Jia-Ping Yan

**Reviewer accepted review:** 2019-05-06 04:44

**Reviewer performed review:** 2019-05-22 05:25

**Review time:** 16 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 checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input 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 type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

This is an important paper tackling important issues in the future prognosis and treatment of pancreatic cancer. Rigorous statistical methods have been applied. It should be published. However, there are marked English grammar mistakes and the whole



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manuscript needs to be re-written by someone with excellent proficiency in English.

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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 48768

**Title:** Integrative analysis of the inverse expression patterns in pancreas development and cancer progression

**Reviewer's code:** 01489017

**Reviewer's country:** Sweden

**Science editor:** Jia-Ping Yan

**Reviewer accepted review:** 2019-05-05 11:54

**Reviewer performed review:** 2019-05-25 06:28

**Review time:** 19 Days and 18 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 checked="" 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 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 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**

The manuscript by Tian and others represents a potentially valuable contribution to the interesting question referring to the connection between (normal) pancreatic development and pancreatic cancer development. Besides the idea that is excellent and



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intelligent, the work falls way behind the potential residing in the data. For once, one would like to know about the expression pattern of the target pathway in the pancreas - normal and diseased - best done by obtaining the also publicly available data in the Human Protein Atlas. Upon superficial check I did, these molecules are expressed in the exocrine pancreas, yes, but in the acing compartment. This needs to be shown and discussed. Furthermore, there are some (admittedly few) data sets out there from PanIN and IPMN. To demonstrate and underscore the genetic evolution towards cancer, the paper would make a much better impact. If decided against it, it needs to be discussed. Minor issues: 1) reference missing last lane on p. 7 (page numbers are also missing!!) when referring to the SOM-SVD. 2) In several figures referring to red-blue colour coding is in a way misleading as part of the figure is a heat map which is red-green (as it is correctly depicted). The blue of course refers to the RIGHT part of the picture(s).

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