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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 6867
Title: Cancer stem cells: involvement in pancreatic cancer pathogenesis and cancer therapeutics perspectives
Reviewer code: 02446104
Science editor: Qi, Yuan
Date sent for review: 2013-10-30 19:23
Date reviewed: 2013-11-08 16:14

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
The authors summarized the research in the literature regarding cancer stem cells (CSCs) in pancreatic cancer pathogenesis and the role of CSCs as a potential target for pancreatic cancer therapy. Overall, it is an interesting topic and the whole article is well-organized. The manuscript provides useful information to researchers and clinicians working in the field of tumor/stem cell biology. The manuscript may be enhanced by including the relationship between the dysregulated microRNAs and CSC-like cells in pancreatic cancer. It will be helpful for the readers to have a fuller view of the MiRNAs regulators in pancreatic cancer.

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ESPS Peer-review Report
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
This is a good and thorough review focusing on cancer stem cells in the pathogenesis and therapies in pancreatic cancer. The contents are relevantly updated with appropriate references. There are two minor topographical mistakes needed to be changes: 1. On page 10 last two lines the word remarcably should be "remarkably" and also "non-metastatic" is the right word. 2. Page 11, This process appears to "be" regulated.... And also ...is also "acted".. also on page 17, et all should be "et al." There may be other mistakes needed to be check through out the text.

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ESPS Peer-review Report
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

The paper by Cristiana Pistol Tanase et al reviewed pathogenesis and therapy of pancreatic cancer focused on the cancer stem cell (CSC) model. The paper deserve attention due to the extensive and clear revision. However, there are points to clarify. Major comments: 1) The paradigm of cancer-initiating stem cells has initially been developed with respect to blood cancers where chronic conditions such as myeloproliferative neoplasms are due to mutations acquired in hematopoietic stem cells [7] The concept of CSCs and cancer-initiating cells (cells of origin) are two separate concepts. Indeed as reviewed in Nature by Visvadier JE (Nature 2011): cancers of distinct subtypes within an organ may derive from different 'cells of origin'. These cells acquire the first genetic hit or hits that culminate in the initiation of cancer. It is important to note that the cell of origin, the normal cell that acquires the first cancer-promoting mutation(s), is not necessarily related to the cancer stem cell (CSC), the cellular subset within the tumour that uniquely sustains malignant growth. That is, the cell-of-origin and CSC concepts refer to cancer-initiating cells and cancer-propagating cells, respectively. Although the tumourinitiating cell and the CSC have been used interchangeably, thetumour-initiating cell more aptly denotes the cell of origin. Please consider this clear and important distintiction and specify accordingly in the paper. 2) Figure 1 Factors involved in occurence of cancer stem cells. The emergence of mutations and aberrant signaling in normal stem cells, progenitors or differentiated cells triggers the transformation of normal cells into cancer stem cells, losing control of cell division. This figure does not reflect clearly the CSC model. Indeed, it does not emerge any gerarchy existing among the cells in the tumour mass that is a key finding of this model. Moreover also it does not emerge the mechanisms determining the inter-tumoral

eterogeneity of the cancers that based on the cells of origin. Indeed wheter a tumor will originate from a stem cells it will determine a more aggressive tumor phenotype with respect a tumor originating from mature cells (see Visvadier JE Nature 2011) Minor comments: 1) The main risk factors for pancreatic cancer include increasing age, smoking, chronic pancreatitis, diabetes mellitus, metabolic syndrome, low levels of serum vitamin D, family history of pancreatic cancer and rare inherited genetic conditions such as Peutz-Jeghers syndrome, familial melanoma and hereditary pancreatitis. Please indicathe references of this sentence. 2) High mortality rate of pancreatic cancer is due to difficulty in early diagnosis and its notorious resistance to chemotherapy and radiation. Please indicate the reference of this sentence. 3) Lack of clinical symptoms in early stages leads to delay in tumor detection; thus, approximately 80% of patients with pancreatic cancer have a metastatic disease at the moment of diagnosis. Please indicate the reference of this sentence. 4) The paradigm of cancer-initiating stem cells has initially been developed with respect to blood cancers where chronic conditions such as myeloproliferative neoplasms are due to mutations acquired in hematopoietic stem cells [7]. It seems the ref is not appropriate with respect the citation 5) 24049451, 12629218, 22956869; What are the meanings of these numbers? 6) Pag. 9 in vitro and in vivo in italic form 7) Please describe briefly the anti-tumoral mechanisms of action of salinomycin.