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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Stem Cells

ESPS manuscript NO: 12825

Title: Mitochondria as therapeutic targets for cancer stem cells

Reviewer code: 00396997

Science editor: Yue-Li Tian

Date sent for review: 2014-07-27 23:15

Date reviewed: 2014-08-13 03:19

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This is well-written comprehensive review / perspective manuscript regarding to cancer stem cell mitochondria and their potential for therapeutic targets. The Authors have a good reputation in this field and their manuscript is indeed well organized. While this reviewer believes that this manuscript is interesting and is dealing with hot topics, the manuscript could be improved through incorporation of the following suggestions, which will increase the overall the impact of this review article.

1. It is better to emphasize more about what is the difference of cancer mitochondria and non-cancer mitochondria. There is a one figure for explaining antioxidant and oxidative phosphorylation systems in mitochondria, but it is also helpful for the readers if there is a schematic diagram or summary table to show this difference, which is also important to understand
2. In page 10, the author mentioned that “most experts agree that effective anti-cancer drugs should be targeted toward CSCs in addition to general cancer cells”. What is the advantage to use mito-target drug to kill CSCs instead of using general anti-cancer drug? What is the key to develop the mito-target drug which can affect to both common cancer cells and CSCs?



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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Stem Cells

ESPS manuscript NO: 12825

Title: Mitochondria as therapeutic targets for cancer stem cells

Reviewer code: 01558248

Science editor: Yue-Li Tian

Date sent for review: 2014-07-27 23:15

Date reviewed: 2014-08-26 09:14

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input checked="" type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

Try to make a table to show the differences of mitochondria in normal stem cell, cancer cell and cancer stem cell for reader to understand the purpose of this article.



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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Stem Cells

ESPS manuscript NO: 12825

Title: Mitochondria as therapeutic targets for cancer stem cells

Reviewer code: 01919991

Science editor: Yue-Li Tian

Date sent for review: 2014-07-27 23:15

Date reviewed: 2014-08-26 21:48

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input checked="" type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

The review deals with a very hot issue: the cancer stem cell mitochondria and their potential for therapeutic targets in oncology. The manuscript is well planned and written, however, a table or scheme pointing out the differences in mitochondrial properties between stem cells (SCs) and cancer stem cells (CSCs) could help the reader and improve the manuscript. In addition, I suggest to cite and integrate in the review the following reference on the new strategies, methods and discoveries to support the actual cancer therapies with novel ones targeted to mitochondrial activity in CSCs: Loureiro et al, Recent Pat Endocr Metab Immune Drug Discov 2013; 7: 102-114 [PMID: 23360288].



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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Stem Cells

ESPS manuscript NO: 12825

Title: Mitochondria as therapeutic targets for cancer stem cells

Reviewer code: 00225340

Science editor: Yue-Li Tian

Date sent for review: 2014-07-27 23:15

Date reviewed: 2014-08-08 01:38

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
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<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This manuscript deal with a topical aspect of oncology, the cancer stem cell. Specifically, it stresses the potential therapeutic role of drug targeting mitochondrial metabolism on this pathogenically relevant cancer cell. The intent is good but some aspects seem not sufficiently treated to give a real idea of the complexity of the CSC metabolism pathophysiology. I would like to recommend to Autors to reinforce some concepts, like: ? Considering the role of the niche in particular and of microenvironment more in general some data about metabolic interrelationshpis should be added (i.e., Morrison, Nature, 505, 327, 2014) ? A dissertation on cancer and mitochondria metabolism should have some notes on the role of mitophagia. ? A deepened discussion on mitochondrial metabolism should ameliorate the understanding of the particular topic (see review by Moreno-Sanchez on BBA Rev on Cancer), the same consideration could be interesting for the antioxidant status of CSCs (see review by Scatena et al on BBA Rev on Cancer); ? An hint of the contradictory results with drugs targeting CSCs (see studies published on N Engl J Med) could reinforce the potentialuse of “antimitochondrial drugs”; ? At last, a more careful description of picture of different cells that can produce CSCs is imperative (see also Visvader et al, reference 2 of the manuscript).