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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 6588
Title: Somatic alterations in mitochondrial DNA and mitochondrial dysfunction in gastric cancer progression
Reviewer code: 00504653
Science editor: Ma, Ya-Juan
Date sent for review: 2013-10-25 18:55
Date reviewed: 2013-10-28 04:07

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] 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 review is generally well-written and covers an emerging and somewhat controversial topic of the role of somatic mtDNA mutations in cancer in general, and in gastric cancer in particular. However, it can benefit from some language editing and from being more inclusive of alternative viewpoints. Specific comments: (1) the statement that "50% of the identified somatic point mutations in the protein-coding region and the tRNA genes of mtDNA of gastric cancer are potentially harmful mutations" suggests a global conclusion about all mtDNA mutations in gastric cancer. Since this conclusion is based on a single study in which a limited number of mutations was analyzed, this reviewer would like to suggest conducting a similar analysis of mtDNA mutations reported in other studies and to report the outcome in a table format. (2) While earlier studies indeed reported that "the steady-state levels of oxidative damage to mtDNA are several-fold higher than that to nuclear DNA [54-56]", more recent studies (see e.g.. Free Radic Biol Med (1999): 27, 456–462; FASEB J (2000):14,355–360; Ann NY Acad Sci (2005): 1042, 210–220) indicate that steady-state levels of oxidative damage in nuclear and mitochondrial DNA are similar. This needs to be acknowledged to avoid bias. (3) The authors should consider incorporating into review not only arguments for the possible increased oxidative damage to mtDNA, but also challenges to the validity of these arguments (see e.g. FEBS J. (2009): 5768-87). Specifically, it has been pointed out that oxidative damage is repaired predominantly by the Base Excision Repair pathway, in which mitochondria are proficient. Moreover, there is evidence that the oxidative lesion 8-oxoguanine is repaired more efficiently in mtDNA than in nDNA (see previous reference). (4) It may be beneficial to clarify how a general defect in DNA polymerase gamma leads to localized mutations in the D-loop

and not elsewhere in the mitochondrial genome. (5) It may benefit readers to acknowledge that oxidative damage can result in >20 different DNA lesions, some of which can result in transition mutations.

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ESPS Peer-review Report
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[Y] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[Y] Accept
[ ] Grade B (Very good)	[ ] 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	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
In this review, authors summarize recent findings of the somatic mtDNA alterations identified in gastric cancers, and their relationships with the clinicopathological features of this cancer. They suggest that point mutation and a decrease in copy number of mtDNA are the two most common mtDNA alterations and might result in mitochondrial dysfunction in gastric cancers. The search for strategies to prevent the mtDNA alterations and to block the mitochondrial retrograde signalingwill benefit the development of novel treatments for this and other malignancies. this review is rational and good.

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[Y] 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 should summarize the views or results of the references,rather than superimposing the original literature content.They should make the review more clear to the readers.They should cite the latest related articles as much as possible.