

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**ESPS manuscript NO:** 27731

**Title:** Regulation of mitochondrial function and endoplasmic reticulum stress by nitric oxide in pluripotent stem cells

**Reviewer's code:** 00609371

**Reviewer's country:** United States

**Science editor:** Xue-Mei Gong

**Date sent for review:** 2016-06-17 14:10

**Date reviewed:** 2016-06-21 05:27

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

This article intends to review the roles of nitric oxide in regulating the mitochondrial function and endoplasmic reticulum stress, especially in pluripotent stem cells. The topic, i.e., NO levels, ER stress and mitochondrial dysfunction could regulate the stem cell fate, is interesting, but the concerns are: 1) The whole article is unbalanced, with a too long INTRODUCTION (almost 5 pages long). 2) The 2nd part of the article, i.e., NO AND MITOCHONDRIAL BIOGENESIS, is also too long, since, this part should not be the major focus of the article, even though it may be necessary. 3) Overall, even the major take home message is well received, the underlying rationale/logic should be tighter, the language needs to be polished, and the flow of the idea should be more natural.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**ESPS manuscript NO:** 27731

**Title:** Regulation of mitochondrial function and endoplasmic reticulum stress by nitric oxide in pluripotent stem cells

**Reviewer's code:** 00202286

**Reviewer's country:** United States

**Science editor:** Xue-Mei Gong

**Date sent for review:** 2016-06-17 14:10

**Date reviewed:** 2016-06-22 00:47

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

The manuscript by Caballano-Infantes et al. is an interesting review about the role of NO in pluripotent stem cells. More particularly, the authors have focused on the modulation of the mitochondrial function and endoplasmic reticulum stress in pluripotent stem cells by NO. The paper is well structured and generally well written. There are however several typos and grammatical errors that need to be corrected/edited.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**ESPS manuscript NO:** 27731

**Title:** Regulation of mitochondrial function and endoplasmic reticulum stress by nitric oxide in pluripotent stem cells

**Reviewer's code:** 02446027

**Reviewer's country:** United States

**Science editor:** Xue-Mei Gong

**Date sent for review:** 2016-06-17 14:10

**Date reviewed:** 2016-07-04 11:57

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

The authors review the role of NO on mitochondrial function and ERS in pluripotent stem cells. The authors also described the mechanism by which NO regulates embryonic development and signaling pathways. The topic is of considerable interest since NO has important role in controlling differentiation and survival on the embryonic stem cells, but the molecular mechanisms by which it modulates these functions unknown. Therefore, review on the relation between NO levels, ER stress and mitochondrial dysfunction that control stem cell fate and the molecular mechanisms by which it modulates these functions is a beneficial. Overall the review is complete, and contains the most important information about the role of NO on mitochondrial function and ERS in stem cells. However, there are several concerns about the manuscript, and needs to be improved. Therefore, I cannot recommend acceptance of the manuscript in its present form. I believe that the manuscript will be suitable for publication in the Journal after minor revision. Minor Comments: 1. The manuscript is long, and there are some typo errors that require attention. 2. During the first occurrence of an acronym, should spell out a technical term first and then present



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the acronym abbreviation in parentheses and use the abbreviation only after that. For example, on page 3, the authors should spelled out human embryonic stem cells first and then abbreviated (hESc), and then on page 10 should use abbreviation only. Some more of these examples can be found throughout the manuscript. The authors should go over the entire manuscript for this correction. 3. Some of the references were old. For example, reference number 4, 30, 53, ext. The authors need to add new, up-to-date references to the reference section. 4. Figure 1 legend is not complete and needs to explain more detail.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**ESPS manuscript NO:** 27731

**Title:** Regulation of mitochondrial function and endoplasmic reticulum stress by nitric oxide in pluripotent stem cells

**Reviewer's code:** 02446280

**Reviewer's country:** Russia

**Science editor:** Xue-Mei Gong

**Date sent for review:** 2016-06-17 14:10

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<input type="checkbox"/> High priority for publication
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		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

The manuscript entitled Regulation of mitochondrial function and endoplasmic reticulum stress by nitric oxide in pluripotent stem cells by Caballano-Infantes et al addresses very interesting issue of undifferentiated cells metabolism and NO involvement in pluripotency maintenance. The manuscript is interesting however there are some drawbacks that makes it difficult to read. Firstly it is a huge number of abbreviations that are used sometimes only once like TEM transmission electron microscopy or instead are used very often like embryonic stem cells (or PGC-1a) but each time providing both full and abbreviated (ESCs) forms. Some abbreviations are not explained (RER???). I would recommend to Authors to read the manuscript carefully and remove all unimportant abbreviations however to combine all meaningful abbreviations on one page. It is also surprised me that in PSCs mitochondria are large (see section 1.4)