

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 23416

**Title:** Aneuploidy in stem cells: A deadly CIN

**Reviewer's code:** 00180736

**Reviewer's country:** Spain

**Science editor:** Jin-Xin Kong

**Date sent for review:** 2015-11-23 22:11

**Date reviewed:** 2015-12-03 03:17

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
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

## COMMENTS TO AUTHORS

The article is very interesting and it puts the emphasis on a problem that may be essential in cellular therapy. However, there are sections that limit the interest reader such as those related to CIN in brain or liver. They should be deleted or summarized. Similar with the paragraph about Down syndrome. It would be desirable to include in the section "types of stem" a table with the most common chromosomal alterations were found in each cell type. Conclusion is very interesting but What happens to the cell therapies with adult cells (mesenchymal, hematopoietic...)?

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 23416

**Title:** Aneuploidy in stem cells: A deadly CIN

**Reviewer's code:** 00203715

**Reviewer's country:** Germany

**Science editor:** Jin-Xin Kong

**Date sent for review:** 2015-11-23 22:11

**Date reviewed:** 2015-12-17 20:48

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input 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"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		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

Martinez et al. "Aneuploidy in stem cells: a deadly CIN" describe chromosomal instability (CIN) in healthy tissues and in pathologies. The authors use several examples to show that CIN is hardly tolerated by stem cells while it can be quite common in differentiated cells like in hepatocytes. In addition, chromosomal instability is raised in aged cells and is dramatically increased in tumors. This will affect the rising field of induced pluripotent stem cells. Although CIN will reduce the proliferation and survival of iPSC, subtle chromosomal arrangements might still be inherited. This risk is even increased with transient ex vivo culture. The review points out that verification of chromosomal fidelity will be a crucial issue for regenerative medicine. The topic chosen is interesting and the manuscript is very well written, concise, clear, and comprehensive.

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 23416

**Title:** Aneuploidy in stem cells: A deadly CIN

**Reviewer's code:** 02446158

**Reviewer's country:** Belgium

**Science editor:** Jin-Xin Kong

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input 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 checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

## COMMENTS TO AUTHORS

The current review proposed by Martinez et al, deals with the description of the role that aneuploidy plays in controlling the number and the quality of somatic and stem cells. The topic of the proposed review is quite interesting and actualized for the field of cell therapy and regenerative medicine. The review is easily readable and well written. However, some parts of the manuscript need more comprehensive and updated details. The authors should address the concerns detailed here below before a publication: - The introduction part should be more developed. A transition paragraph from somatic to stem cells is to add. - The authors should provide additional data regarding the description of aneuploidy in cell types and in the different zones (proximal and/or distal to the corresponding niches) of the discussed organs (brain and liver)? - Is there any correlation between potency level and aneuploidy? or between proliferation rate and aneuploidy? Indeed, these features represent the principal differences between embryonic vs somatic stem cells. Is the quality of differentiation in stem cells impacted by aneuploidy? - In the liver, when hepatocytes are no more able to proliferate and stem cells are emerging, is there any documented data involving aneuploidy? A brief liver disease section is to add if documented data related to aneuploidy are available -



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Because mesenchymal stem cells (MSC) have been currently used in many clinical trials, a comparison with ESC and iPSCs should be added. - A brief description of the technical skills that have been/are used for an accurate analysis of aneuploidy should be added. A table would be more appreciated. - Is there any difference in the aneuploidy molecular level/markers during development? Are the differences observed between somatic and stem cells equivalent in all tissues? This information is very important regarding an accurate comparison with what is described in vitro. - The authors only propose Nanog transcription factor as aneuploidy driver, other demonstrated and/or proposed factors should be discussed if any - Typographical errors should be corrected.