

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Stem Cells

ESPS manuscript NO: 13241

Title: Connexin mutant embryonic stem cells and human diseases

Reviewer code: 01217232

Science editor: Fang-Fang Ji

Date sent for review: 2014-08-13 18:12

Date reviewed: 2014-08-17 10:10

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input checked="" type="checkbox"/> [Y] Grade A: Excellent	<input checked="" type="checkbox"/> [Y] Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> [Y] Accept
<input type="checkbox"/> [] Grade B: Very good	<input 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	<input type="checkbox"/> [] Existing	<input type="checkbox"/> [] Minor revision
<input type="checkbox"/> [] Grade E: Poor		<input type="checkbox"/> [] No records	<input type="checkbox"/> [] Major revision

COMMENTS TO AUTHORS

In this review, the authors have summarized the original investigations on mouse Cx knockout models and the potential significance in the development of human diseases. Generally, the review has been appropriately prepared and it is easily readable.

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Stem Cells

ESPS manuscript NO: 13241

Title: Connexin mutant embryonic stem cells and human diseases

Reviewer code: 02446219

Science editor: Fang-Fang Ji

Date sent for review: 2014-08-13 18:12

Date reviewed: 2014-08-25 02:43

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existing	<input checked="" 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	<input type="checkbox"/> Existing	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

it might be a good idea that the authors summarize the findings and conclude at the end .

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Stem Cells

ESPS manuscript NO: 13241

Title: Connexin mutant embryonic stem cells and human diseases

Reviewer code: 02446062

Science editor: Fang-Fang Ji

Date sent for review: 2014-08-13 18:12

Date reviewed: 2014-08-28 23:06

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 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	<input type="checkbox"/> Existing	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

Nishii et al reviewed the application of knockout mice, mouse embryonic stem cells and human induced pluripotent stem cells to studying the unique role that each connexin isoform plays. Overall this is a well-written review and sounds original. However, there are several points that are confusing and need to be clarified. Specific concerns and suggestions are provided below.

1. The last sentence in the Core tip on page 3 is confusing because it gives an impression that Cx43 and Cx45 mutant mouse embryonic stem cells need to be generated in the future, and states the mutant ESCs could be a model for human iPSCs that is another model to understand human diseases. Perhaps it will be better to state that according to the studies using mutant mouse ESCs, Cx43 or Cx45-null human iPSCs may become a useful model.
2. On line 11, page 4, at the blastocyst stage, there are two types of trophoblasts, polar and mural trophoctoderm. Perhaps the one making gap junctions with both trophoblasts and the inner cell mass cells will be the polar trophoctoderm.
3. If known, the reason why no Cx23 and Cx33 knockout mice have been generated needs to be provided on line 14, page 5.
4. The statement starting on line 6, page 6, is confusing because apparently some of Cx isoforms play unique function in a specific cell type. Perhaps, it will be better to state that a specific individual Cx does not seem to possess a one-to-one association with a unique cell type in vivo.
5. The statement starting on line 15, page 6, is not accurate. Those constitutive KO mice were never born due to embryonic lethality.
6. Perhaps "present with" on line 2, page 7, is meant for "exhibit".
7. The statement on line 2, page 9, can be more specific and informative. For example, "attempts to

mutate a unique Cx isoform in a tissue specific manner have been made". 8. On line 14 page 9, the use of "researchers" as a subject is not advised in the review article like this. Instead of "researchers sometimes want to", "it has been of great interest to" is suggested. 9. On line 13, page 10, "Cx45-KO mice" are supposed to carry conditional alleles. Because in this chapter conditional KO approaches are introduced, it is advised to make a clear distinction between constitutive and conditional alleles. 10. Sentences starting on line 14, page 10, are redundant. In particular, the sentence starting from "Taken together" can be revised to, for example, "Taken together, the heart abnormalities are expected to be the primary defect associated with the loss of Cx45 in developing embryos." 11. On line 12, page 11, why are only "several" but not "many" mouse genetic models useful to derive iPSCs from? Is the word "several" necessary in this sentence? 12. On line 15, page 11, reference 58 is a review article. In this context, the original studies need to be cited. 13. Table 1. What is the "partial embryonic lethality"? This needs to be defined. 14. The figure legends must be elaborated. What does the green highlight indicate? What are the middle and right cartoons and their differences between A and B? What are the middle and right cartoons in C?