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# ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology
**ESPS manuscript NO:** 15701
**Title:** Hepatocytes from Fibroblasts-The Truth and Myth of Transdifferentiation
**Reviewer's code:** 02519850
**Reviewer's country:** India
**Science editor:** Yuan Qi
**Date sent for review:** 2014-12-05 16:43
**Date reviewed:** 2015-01-18 14:04

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|---|---|---|---|
| [ ] Grade A: Excellent | [ ] Grade A: Priority publishing | PubMed Search: | [ ] Accept |
| [ ] Grade B: Very good | [Y] Grade B: Minor language polishing | [ ] The same title | [ ] High priority for publication |
| [Y] Grade C: Good | [ ] Grade C: A great deal of language polishing | [ ] Duplicate publication | [ ] Rejection |
| [ ] Grade D: Fair | [ ] Grade D: Rejected | [ ] Plagiarism | [ ] Minor revision |
| [ ] Grade E: Poor | | [Y ] No | [ Y] Major revision |
| | | BPG Search: | |
| | | [ ] The same title | |
| | | [ ] Duplicate publication | |
| | | [ ] Plagiarism | |
| | | [Y ] No | |

## COMMENTS TO AUTHORS

I have read and reviewed the manuscript. It made an interesting reading. The author has compared the two available methods of obtaining hepatocytes either directly by transdifferentiation of fibroblasts into hepatocytes or directed differentiation of ES/iPS cells. They point out that ES/iPS cells differentiation remains inefficient, convert into immature cells and fail to integrate in host. Whereas the transdifferentaition process is also inefficient. Author has then listed out various problems which may occur with the concept of transdifferentiation and thus concludes that iPS cells will be best candidates for regenerating the liver in future - once protocols are modified. He has very nicely given the example of melting metal to get new goods rather than compressing metal into new forms without melting. It is already 15 years hES cells and 8 years of iPS cells - how much more time is required to evolve a novel protocol for differentiation of ES/iPS cells? It is easy and cheaper to expand fibroblasts in large numbers compared to iPS cells - thus the argument taht iPS cells area better source of fibroblasts is redundant and should be deleted. I would like the author to introduce another player in their article - VSELs which may exist as a sub-population in skin fibroblast culture and may indeed be undergoing differentiation (thus only 0.3% of MEFs

convert into iHEP). They may wish to refer to a recent article http://www.ncbi.nlm.nih.gov/pubmed/25545634. This will then make a complete review ... If authors are convinced that a sub-population of cells in fibroblast culture get differentiated - all the concerns of epigenetic memory/telomere resetting etc will cease to exist. Also because of the quiescent nature, VSELs do not accumulate mutations over time. Author may refer to Fig 1a of the manuscript by Sekiya and Suzuki 2011- a sub-population of VSELs in fibroblast culture is clearly observed. http://www.ncbi.nlm.nih.gov/pubmed/21716291 I will be willing to review the article provided all these suggestions get incorporated

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# ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology
**ESPS manuscript NO:** 15701
**Title:** Hepatocytes from Fibroblasts-The Truth and Myth of Transdifferentiation
**Reviewer's code:** 02444774
**Reviewer's country:** China
**Science editor:** Yuan Qi
**Date sent for review:** 2014-12-05 16:43
**Date reviewed:** 2015-03-05 10:45

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|---|---|---|---|
| [ Y] Grade A: Excellent | [ Y] Grade A: Priority publishing | PubMed Search: | [ Y] Accept |
| [ ] Grade B: Very good | [ ] Grade B: Minor language polishing | [ ] The same title | [ ] High priority for publication |
| [ ] Grade C: Good | [ ] Grade C: A great deal of language polishing | [ ] Duplicate publication | [ ] Rejection |
| [ ] Grade D: Fair | [ ] Grade D: Rejected | [ ] Plagiarism | [ ] Minor revision |
| [ ] Grade E: Poor | | [Y ] No | [ ] Major revision |
| | | BPG Search: | |
| | | [ ] The same title | |
| | | [ ] Duplicate publication | |
| | | [ ] Plagiarism | |
| | | [Y ] No | |

## COMMENTS TO AUTHORS

This was a very nice written review article by an expert in the field.

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# ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology
**ESPS manuscript NO:** 15701
**Title:** Hepatocytes from Fibroblasts-The Truth and Myth of Transdifferentiation
**Reviewer's code:** 01560464
**Reviewer's country:** China
**Science editor:** Yuan Qi
**Date sent for review:** 2014-12-05 16:43
**Date reviewed:** 2015-03-09 16:12

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|---|---|---|---|
| [ ] Grade A: Excellent | [ ] Grade A: Priority publishing | PubMed Search: | [ ] Accept |
| [Y] Grade B: Very good | [Y] Grade B: Minor language polishing | [ ] The same title | [ ] High priority for publication |
| [ ] Grade C: Good | [ ] Grade C: A great deal of language polishing | [ ] Duplicate publication | [ ] Rejection |
| [ ] Grade D: Fair | [ ] Grade D: Rejected | [ ] Plagiarism | [Y] Minor revision |
| [ ] Grade E: Poor | | [Y] No | [ ] Major revision |
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| | | [ ] The same title | |
| | | [ ] Duplicate publication | |
| | | [ ] Plagiarism | |
| | | [Y] No | |

## COMMENTS TO AUTHORS

1) The review introduced the several protocols which claim generation of hepatocyte like cells from directed differentiation embryonic stem cells (ES), induced pluripotent stem cells (iPSCs) or other cell types(such as fibroblasts). The authors compared the advantages and disadvantages of the several protocols. It is better guidence to know about the derivation of hepatocyte like cells and therapeutic method for the acute or chronic liver dysfunction. 2) The review has had a lot of introduction about the generation of hepatocyte like cells from ES and iPSCs. But there is less introduction about hepatocyte like cells derived directly from fibroblasts by transdifferentiation). 3) It need supply the content of hepatocyte like cells derived directly from fibroblasts by transdifferentiation. The advantages and disadvantages of generation of hepatocyte like cells by transdifferentiation and the viewpoint of authors should be supplied .