

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 67533

Title: Impact of senescence on the trans-differentiation process of human hepatic progenitor-like cells

Reviewer's code: 05923483

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Italy

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Reviewer chosen by: AI Technique

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The manuscript entitled “Impact of senescence on the trans-differentiation process of human hepatic progenitor-like cells” reported by Bellanti F et al. investigated the effects of senescence on the trans-differentiation capacity and mitochondrial metabolism of the human HepaRG cells. Overall, the manuscript is well-constructed and it provide valuable information to the readers. Following are some suggestions for the authors.

1. For the study of liver metabolism and hepatic progenitors using trans-differentiated HepaRG cell line, the functions of hepatocyte-like cells are important. In Figure 3, besides of gene expression, albumin secretion capacity, activities of CYP3A4 and γ -glutamyl transpeptidase should be investigated. Or at least, the protein level of these candidates should be presented by Western-blotting or immunofluorescence staining.
2. How are the expressions of markers of both progenitor and differentiated cells (such as CD49a, CD49f, CD184, EpCAM and CK19) in P10 and P20 HepaRG cells before 2-week DMSO exposure? The changes of the expression of these markers will represent the trans-differentiation process.
3. In page 9, line 281. “Figure 2A” is supposed to be “Figure 4A”.