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# PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology
**Manuscript NO:** 39310
**Title:** Taking advantage of the potential of mesenchymal stromal cells in liver regeneration: cells and extracellular vesicles as therapeutic strategies
**Reviewer's code:** 02702057
**Reviewer's country:** Italy
**Science editor:** Xue-Jiao Wang
**Date sent for review:** 2018-04-13
**Date reviewed:** 2018-04-14
**Review time:** 1 Day

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|---|---|---|---|
| [ ] Grade A: Excellent | [ Y] Grade A: Priority publishing | Google Search: | [ ] Accept |
| [ Y] 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 | [ Y] Minor revision |
| [ ] Grade E: Poor | | [ Y ] No | [ ] Major revision |
| | | BPG Search: | |
| | | [ ] The same title | |
| | | [ ] Duplicate publication | |
| | | [ ] Plagiarism | |
| | | [ Y ] No | |

## COMMENTS TO AUTHORS

Manuscript titled "Taking advantage of the potential of mesenchymal stromal cells in liver regeneration: cells and extracellular vesicles as therapeutic strategies." deals an important issue of Cell-based therapies for acute and chronic liver diseases. This review summarizes the latest results achieved in clinical trials using MSCs as cell therapy for liver regeneration, the role of EVs in liver physiopathology and the potential of MSC-derived EVs as intercellular mediators and therapeutic tools in liver diseases. The work is good, updated, interesting and fluent. Moreover, there are some minor revisions to be addressed before to accept it for publications. Please strengthen, improve and update better the introduction section adding more details and interesting information on: • (first paragraph) non-alcoholic fatty liver disease: 4Ps medicine of the fatty liver: the research model of predictive, preventive, personalized and participatory

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medicine-recommendations for facing obesity, fatty liver and fibrosis epidemics. EPMA J. 2014 Dec 7;5(1):21. Echocardiography and NAFLD (non-alcoholic fatty liver disease). Int J Cardiol. 2016 Oct 15;221:275-9. Fatty liver disease and lifestyle in youngsters: diet, food intake frequency, exercise, sleep shortage and fashion. Liver Int. 2016 Mar;36(3):427-33. • (second paragraph) different source of MSC such as adipose tissue and other possible tissue engineering applications: Asymmetrical seeding of MSCs into fibrin-poly(ester-urethane) scaffolds and its effect on mechanically induced chondrogenesis. J Tissue Eng Regen Med. 2017 Oct;11(10):2912-2921. Chondrocyte and mesenchymal stem cell-based therapies for cartilage repair in osteoarthritis and related orthopaedic conditions. Maturitas. 2014 Jul;78(3):188-98. Mesenchymal stem cells from adipose tissue which have been differentiated into chondrocytes in three-dimensional culture express lubricin. Exp Biol Med (Maywood). 2011 Nov;236(11):1333-41. I recommend to see the above recent and interesting papers or others and quote and comment them to stay to the study topic. Please improve the conclusion section: please specify the clinical relevance of your work, the rational of this work, innovation, limitations, your critical view and some important suggestions for the scientific community.

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**Name of journal:** World Journal of Gastroenterology
**Manuscript NO:** 39310
**Title:** Taking advantage of the potential of mesenchymal stromal cells in liver regeneration: cells and extracellular vesicles as therapeutic strategies
**Reviewer's code:** 00609434
**Reviewer's country:** Italy
**Science editor:** Xue-Jiao Wang
**Date sent for review:** 2018-04-13
**Date reviewed:** 2018-04-14
**Review time:** 1 Day

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| [Y ] Grade A: Excellent | [ Y] Grade A: Priority publishing | Google Search: | [ ] 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 | [ Y] Minor revision |
| [ ] Grade E: Poor | | [ Y ] No | [ ] Major revision |
| | | BPG Search: | |
| | | [ ] The same title | |
| | | [ ] Duplicate publication | |
| | | [ ] Plagiarism | |
| | | [ Y ] No | |

## COMMENTS TO AUTHORS

The manuscript from Fiore et al. is an interesting review describing the current status of the preclinical and clinical protocols investigating the use of MSCs in liver diseases. Furthermore it focuses on MSC-derived secretome and extracellular vesicles therapeutic potentials. The review is very interesting and updated in its collection and description of all the clinical protocols for liver diseases envisioning the use of either autologous or allogeneic MSCs. I find it worthy of publication quite in its actual form, however I find very difficult to read Figure 2 due to the reduced size of the characters. The authors should improve the output of the Figure for a better understanding.

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**Name of journal:** World Journal of Gastroenterology
**Manuscript NO:** 39310
**Title:** Taking advantage of the potential of mesenchymal stromal cells in liver regeneration: cells and extracellular vesicles as therapeutic strategies
**Reviewer's code:** 02567328
**Reviewer's country:** Italy
**Science editor:** Xue-Jiao Wang
**Date sent for review:** 2018-04-13
**Date reviewed:** 2018-04-14
**Review time:** 1 Day

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| [ ] Grade E: Poor | | [ Y ] No | [ ] Major revision |
| | | BPG Search: | |
| | | [ ] The same title | |
| | | [ ] Duplicate publication | |
| | | [ ] Plagiarism | |
| | | [ Y ] No | |

## COMMENTS TO AUTHORS

In the manuscript "Taking advantage of the potential of mesenchymal stromal cells in liver regeneration: cells and extracellular vesicles as therapeutic strategies" the authors reviewed the literature about the use of mesenchymal stem cells (MSCs) and extracellular vesicles (EVs) released by MSCs in liver diseases and regeneration. The topic is very interesting but recently (2017-2018) many reviews have been published concerning this subject, some of which are not reported in the references. In my opinion the proposed manuscript does not add anything new to what is in the literature. Examples of review not reported in references: - Role of mesenchymal stem cells, their derived factors, and extracellular vesicles in liver failure. Wang J, Cen P, Chen J, Fan L, Li J, Cao H, Li L. Stem Cell Res Ther. 2017 Jun 6;8(1):137. doi: 10.1186/s13287-017-0576-4. - Mesenchymal Stem/Stromal Cell-Derived Extracellular Vesicles and Their Potential as Novel Immunomodulatory Therapeutic Agents. Börger V, Bremer M, Ferrer-Tur R, Gockeln L, Stambouli O, Becic A, Giebel B. Int J Mol Sci. 2017 Jul 6;18(7). pii: E1450. doi: 10.3390/ijms18071450. - Extracellular vesicles: Novel mediator for cell to cell

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communications in liver pathogenesis. Devhare PB, Ray RB. Mol Aspects Med. 2018 Apr;60:115-122. doi: 10.1016/j.mam.2017.11.001. - Exosomes in liver pathology. Sato K, Meng F, Glaser S, Alpini G. J Hepatol. 2016 Jul;65(1):213-221. doi: 10.1016/j.jhep.2016.03.004. - Historical Perspectives and Advances in Mesenchymal Stem Cell Research for the Treatment of Liver Diseases. Lee CW, Chen YF, Wu HH, Lee OK. Gastroenterology. 2018 Jan;154(1):46-56. doi: 10.1053/j.gastro.2017.09.049. - Cellular Mechanisms of Liver Regeneration and Cell-Based Therapies of Liver Diseases. Kholodenko IV, Yarygin KN. Biomed Res Int. 2017;2017:8910821. doi: 10.1155/2017/8910821.