

Responses to reviewer and editor comments for review article:

Manuscript Number: 81070

Manuscript Type: INVITED REVIEW, ID NUMBER: 03724640

Bioengineering liver tissue by repopulation of decellularised scaffolds

Dear editorial team,

Please find below our point by point responses to the comments from reviewers and editor in chief:

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The review article is very well written and provides detailed information on the topic in a concise manner. The tables are informative and the references are up to date. I would suggest adding a schematic or a figure or two in the review article.

We carefully considered adding figures in the original manuscript to illustrate the processes described in the text, but ultimately decided against this. The reasons for this conclusion were that we were of the opinion that image representations of the subject matter neither added any additional information to the detailed points in the text, nor enhanced the explanation of the concepts and processes described. We feel that in this instance, figures would only repeat available information, and detract from the concise information presented. Respectfully, we would prefer not to add figures, though will oblige if it is insisted on. In this case it would be very helpful to know from the reviewer which aspect of the text would benefit from an image.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This is a well-written manuscript. However, the structure of the manuscript does not match the general format of reviews. Hence, the authors have been advised to revise the headings and subheadings of the manuscript accordingly. For example, instead of the followings: SECTION 7: IMMUNOGENICITY OF DECELLULARISED SCAFFOLDS 7.1: Introduction Write 7: IMMUNOGENICITY OF DECELLULARISED SCAFFOLDS only.

We have made alterations to the headings and subheadings as suggested by reviewer 2

Editor in chief comments

I have reviewed the Peer-Review Report, English Language Editing certificate and the full text of the manuscript, all of which have met the basic publishing requirements of the World Journal of Hepatology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

Using the 'Reference Citation Analysis' tool, and entering 'liver decellularization' as broad search terms, we identified 11 further references shown below. After ranking by Impact Index per article, 8 of the 11 references had a positive score, and the remaining 3 had a nil score. Of the 8 references with a positive score, 3 (shown in green) were already included in the manuscript. Of the remaining 5 references, 4 (shown in blue) were indexed in pubmed and have been added to the manuscript, with appropriate changes to the text (details shown with each reference). The 5th (shown in orange) was not indexed in pubmed and has not been included in the manuscript. The 3 references with a nil score (shown in red) were not included in the manuscript.

1 Maghsoudlou P, Georgiades F, Smith H, Milan A, Shangaris P, Urbani L, Loukogeorgakis SP, Lombardi B, Mazza G, Hagen C, Sebire NJ, Turmaine M, Eaton S, Olivo A, Godovac-Zimmermann J, Pinzani M, Gissen P, De Coppi P. Optimization of Liver Decellularization Maintains Extracellular Matrix Micro-Architecture and Composition Predisposing to Effective Cell Seeding. PLoS One 2016;11:e0155324. [PMID: 27159223 DOI: 10.1371/journal.pone.0155324] [Cited by in Crossref: 51] [Cited by in RCA: 42] [Impact Index Per Article: 8.5] [Reference Citation Analysis] [What about the content of this article? (0)] [Abstract] [Track Full Text] Open 6 51 42
8.5

Already in manuscript

2 Struecker B, Hillebrandt KH, Voithl R, Butter A, Schmuck RB, Reutzel-selke A, Geisel D, Joehrens K, Pickerodt PA, Raschzok N, Puhl G, Neuhaus P, Pratschke J, Sauer IM. Porcine Liver Decellularization Under Oscillating Pressure Conditions: A Technical Refinement to Improve the Homogeneity of the Decellularization Process. Tissue Eng Part C Methods 2015;21:303-13. [DOI: 10.1089/ten.tec.2014.0321] [Cited by in Crossref: 46] [Cited by in RCA: 49] [Impact Index Per Article: 6.6] [Reference Citation Analysis] [What about the content of this article? (0)] [Track Full Text] Open
7 46 49 6.6

Already in manuscript

3 De Kock J, Ceelen L, De Spiegelaere W, Casteleyn C, Claes P, Vanhaecke T, Rogiers V. Simple and quick method for whole-liver decellularization: a novel in vitro three-dimensional bioengineering tool? Arch Toxicol. 2011;85:607-612. [PMID: 21512802 DOI: 10.1007/s00204-011-0706-1] [Cited by in Crossref: 52] [Cited by in RCA: 44] [Impact Index Per Article: 4.7] [Reference Citation Analysis] [What about the content of this article? (0)] [Abstract] [Track Full Text] 11 52
44 4.7

This reference has been added to section 5.2, to complement the existing references to the text.

4 Geerts S, Ozer S, Jaramillo M, Yarmush ML, Uygun BE. Nondestructive Methods for Monitoring Cell Removal During Rat Liver Decellularization. Tissue Eng Part C Methods 2016;22:671-8. [PMID: 27169332 DOI: 10.1089/ten.TEC.2015.0571] [Cited by in Crossref: 27] [Cited by in RCA: 29] [Impact Index Per Article: 4.5] [Reference Citation Analysis] [What about the content of this article? (0)] [Abstract] [Track Full Text] Open 6 27 29 4.5

This reference has been added to section 5.4 and an additional sub-section discussing the work described has been added to the manuscript.

5 Struecker B, Butter A, Hillebrandt K, Polenz D, Reutzel-selke A, Tang P, Lippert S, Leder A, Rohn S, Geisel D, Denecke T, Aliyev K, Jöhrens K, Raschzok N, Neuhaus P, Pratschke J, Sauer IM. Improved rat liver decellularization by arterial perfusion under oscillating pressure conditions: Arterial rat liver decellularization. J Tissue Eng Regen Med 2017;11:531-41. [DOI: 10.1002/term.1948] [Cited by in Crossref: 34] [Cited by in RCA: 38] [Impact Index Per Article: 4.3] [Reference Citation Analysis] [What about the content of this article? (0)] [Track Full Text] 8
34 38 4.3

Already in manuscript

6 Khajavi M, Hashemi M, Kalalinia F. Recent advances in optimization of liver decellularization procedures used for liver regeneration. Life Sci 2021;281:119801. [PMID: 34229008 DOI: 10.1016/j.lfs.2021.119801] [Cited by in Crossref: 1] [Impact Index Per Article: 1.0] [Reference Citation Analysis] [What about the content of this article? (0)] [Abstract] [Track Full Text] 1 1
0 1.0

This reference has been added to section 5.2 and the manuscript text altered accordingly.

7 Lin Y, Wang L, Wang J, Pan L, Zhu G, Liu W, Braddock M, Zheng M. New advances in liver decellularization and recellularization: innovative and critical technologies. *Expert Rev Gastroenterol Hepatol* 2015;9:1183-91. [DOI: 10.1586/17474124.2015.1058155] [Cited by in Crossref: 6] [Cited by in RCA: 6] [Impact Index Per Article: 0.9] [Reference Citation Analysis] [What about the content of this article? (0)] [Track Full Text] 7 6 6 0.9

This reference has been added to section 5.2 and the manuscript text altered accordingly.

8 Fathi I, Eltawila A. Whole-Liver Decellularization: Advances and Insights into Current Understanding. *Xenotransplantation - New Insights* 2017. [DOI: 10.5772/intechopen.69487] [Cited by in Crossref: 2] [Cited by in RCA: 2] [Impact Index Per Article: 0.4] [Reference Citation Analysis] [What about the content of this article? (0)] [Track Full Text] 5 2 2 0.4

Not indexed in Pubmed, and excluded from manuscript.

9 Sibuea CV. Liver Decellularization as Liver Organoid Reconstruction Scaffold. *bul farmatera* 2021;6:6. [DOI: 10.30596/bf.v6i1.4560] [Cited by in Crossref: 0] [Impact Index Per Article: 0] [Reference Citation Analysis] [What about the content of this article? (0)] [Track Full Text] 1 0

Impact score zero, and excluded from manuscript

10 Struecker B, Butter A, Hillebrandt K, Voith R, Polenz D, Reutzel-selke A, Jöhrens K, Geisel D, Raschzok N, Neuhaus P, Sauer I. P1 OSCILLATING PRESSURE CONDITIONS SIGNIFICANTLY IMPROVE RAT AND PIG LIVER DECELLULARIZATION. *J Hepatol* 2014;60:S67. [DOI: 10.1016/s0168-8278(14)60165-3] [Cited by in Crossref: 0] [Impact Index Per Article: 0] [Reference Citation Analysis] [What about the content of this article? (0)] [Track Full Text] 8 0

Impact score zero, and excluded from manuscript

11 Rupert S, Selvaraj S, Malayaperumal S, Ramanathan R, Anbalagan C, Satyanesan J, Vennila R, Rajagopal S. Comparison of Extracellular Matrix (ECM) of Normal and D-Galactosamine-Induced Mice Model of Liver Injury Before and After Liver Decellularization. *Regen Eng Transl Med*

2021;7:405-15. [DOI: 10.1007/s40883-020-00153-3] [Cited by in Crossref: 0] [Impact Index Per Article: 0] [Reference Citation Analysis] [What about the content of this article? (0)] [Track Full Text]
2 0

Impact score zero, and excluded from manuscript

We hope that these alterations to the manuscript are satisfactory and look forward to hearing from you.

Your sincerely,

Emmanuel Huguet

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