

ANSWERING REVIEWERS COMMENTS

January 15, 2015



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 14293-review.doc).

Title: *In utero* and *exo utero* fetal surgery on histogenesis of organs

Author: Esrat Jahan, Ashiq Mahmood Rafiq, Hiroki Otani

Name of Journal: *World Journal of Surgical Procedures*

ESPS Manuscript NO: 14293

The manuscript has been improved according to the suggestions of reviewers:

1. Format has been updated
2. Revision has been made according to the suggestions of the reviewer

(1) 1st reviewer comments:

- 1, This review described the rationale for *in utero* and *exo utero* surgical manipulation of animal models of different kinds of organ defects or anomalies and their repairment based on the analyses of histogenesis of organs and pathologic observations. The manuscript represented an interesting for readers in this scope.
- 2, Many contents of this review were similar with previous published paper(Ngo-Muller V, Muneoka K. *In utero* and *exo utero* surgery on rodent embryos. *Methods Enzymol.* 2010;476:205-26), which should be shorten.
- 3, In this manuscript it was described that intrauterine embryo injections can be successfully carried out on mouse embryo stages as early as E9.5. However, in a

recent published paper showed intrauterine injection could be performed as early as E8.5 (Endo M1, Zoltick PW, Chung DC, Bennett J, Radu A, Muvarak N, Flake AW. Gene transfer to ocular stem cells by early gestational intraamniotic injection of lentiviral vector. *Mol Ther*. 2007 Mar;15(3):579-87. 2, Endo M1, Zoltick PW, Radu A, Jiang Q, Matsui C, Marinkovich PM, McGrath J, Tamai K, Uitto J, Flake AW. Early intra-amniotic gene transfer using lentiviral vector improves skin blistering phenotype in a murine model of Herlitz junctional epidermolysis bullosa. *Gene Ther*. 2012 May;19(5):561-9.). Therefore it is necessary to add many recent published papers in this manuscript.

Reply to the reviewer's comments:

As the reviewer suggested that the similar contents should be shortened, so we have shortened the texts. There was no specifically mentioned contents to be shortened, so the current revised manuscript hopefully be acceptable. From the initial submitted manuscript, we have deleted some parts of the texts, and these are- page 8, line 20-21; page 9, lines 2-6, 9-16, 23, 25-26; page 10, lines 6, 10-17, 20-22; page 11, lines 13-17, 23-26; page 12, line 8-10; page 21, lines 8-9, 25-26; page 22, lines 6-8, 17-18, 22-24; page 23, lines 6-8, 25-26.

I would like to say thanks and appreciate you for your kind information about some latest references. I have added those references in the revised version of the manuscript (page 7, line 15-16) which have been highlighted.

(2) 2nd reviewer comments:

This is a review of fetal surgery on histogenesis of organs in animals, The review is very comprehensive, including in utero and ex utero and covering different animals, an very well written with minimal typo and grammatical errors. Just a few suggestions to highlight the review even higher quality:

1. Title: since the review focus on animals only, it is better to include "**in animals**" at the end. 2. Introduction: page 5, first paragraph, last sentence seems not relevant. No further details was provided in the rest of the review and prevention and treatment

of cardiovascular disease and type 2 diabetes are more maternal than fetal. 3. Ex Utero surgery: it only included rodents, how about other animals, such as sheep, pig and primates as described in In Utero Surgery. 4. Abdominal Closure and Recovery: it is too short in relative to other sections and also only rodents but not other animals. If not much, consider to combine into the former sections.

In addition, how about any figures of survival rates in both mothers and fetus?

5. If possible, a new short section to discuss the prospective and current development of fetal therapy in human.

Reply to the reviewer's comments:

1. Regarding the title; according to the authors' guideline of this journal, the title must be less than 12 words. If we add the word "in animals" as the reviewer suggested, then the title will become 13 words. We appreciate your generous suggestion, but if the honorable editor wish to give permission to add "in animals" at the end of the title then we will welcome it.
2. In the introduction section page 5, the non-relevant sentences have been deleted from the initial submitted manuscript.
3. The novel *exo utero* surgery was done only in rodents and we described this technique details in the manuscript. So far, no reports or published papers have been found for this *exo utero* surgery done in other animals.
4. Regarding the abdominal closure and recovery section, the procedures of the abdominal closer and recovery were similar in both the *in utero* and *exo utero* surgery in rodents. Therefore, we combined it under the common heading of *exo utero* surgery page 26.

We also added sentences explaining the survival rates in page 15, line 13-16.

5. We appreciate your generous suggestion. Although we have done some experimental work on rodents, we do not have any experience in the field of human fetal therapy. So it is difficult for us to write some discussion regarding the prospective and current development of fetal therapy in human, and we refrain from adding the discussion.

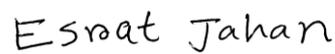
(3) Editor's comments:

"There is no conflict of interest" we have added this sentence in the revised form of the manuscript page 1.

3. References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Surgical Procedures*.

Sincerely yours,



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