We thank the Company editor-in-chief and Reviewers for the overall positive response. We have added additional information to the paper to address all comments. Here we provide a point-by-point response to The Reviewer's comments.

Company editor-in-chief

1. Before final acceptance, the author(s) must add a table/figure to the manuscript.

We added one table and one figure to the manuscript.

2. 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.

We applied a new tool - RCA and introduced a number of new links.

Reviewer 1

1. The title focused on the 4D bioprinting and it is barely reported in the manuscript. I suggest also mentioning the 3D in the title (major part of the manuscript) and also to shorten the title because only 18 words are allowed.

The title of the article has been changed according to your comment. We couldn't use abbreviations in the title. We removed 4D from the title of the manuscript to shorten the title.

"Prospects for the use of olfactory mucosa cells in bioprinting for the treatment of spinal cord injuries"

2. References are not in the right format. Reference [62] is in the right format.

Links are presented in accordance with the example on the journal's website.

3. Each part should be numbered with 1, 1.1 …

The chapters have been numbered according to your recommendations.

4. A figure/graph will help the readers to understand the minireview subject.

The figure1 has been added to the chapter 2 for understanding minireview subject. Figure 1. Dynamics of recovery of hind limb motor activity in rats after transplantation of human OEC alone and in combination with NT-3 into SC cysts. This figure clearly demonstrates that neurotrophin-3 improves the efficiency of cell therapy with ensheathing cells.

5. In the "exogenous neurotrophins Therapy" the authors should mention in 2-3 sentences the potential harmful long term effect of using viruses for gene therapies.

The review considered the delivery of neurotrophic factors using adenovectors. We added text to the chapter 2.

«Special attention should be paid to the safety of this technology. Adenoviral vectors are the most studied in this respect. They are successfully used in the creation of vaccines and treatment of oncological diseases. At present, they are being actively studied for use in regenerative medicine. Although great success has been achieved in this field, it is necessary to improve the immune system

response, the life span of the virus, and the packing ability of the vectors. However, the evolution of the adenoviral vector as a tool for the transfer of genetic material has revolutionized how doctors and scientists can approach the treatment of even the most debilitating diseases [59].

Lee CS, Bishop ES, Zhang R, Yu X, Farina EM, Yan S, Zhao C, Zeng Z, Shu Y, Wu X, Lei J, Li Y, Zhang W, Yang C, Wu K, Wu Y, Ho S, Athiviraham A, Lee MJ, Wolf JM, Reid RR, He T-C. Adenovirus-mediated gene delivery: Potential applications for gene and cell-based therapies in the new era of personalized medicine. Genes Dis 2017; 4: 43–63. [PMID: 28944281 DOI: 10.1016/j.gendis.2017.04.001]

6. Injection rather than "by their direct introduction".

We wrote "Injection" instead of "by their direct introduction".

Reviewer 2

1. What are the limitations of olfactory mucosa cells for transplantation that deserve attention? Feasibility and safety of cell-based treatments should also be discussed.

We added text to the chapter 1.

«Despite the fact that cell-therapy based on olfactory mucosa cells is one of the most promising treatments for spinal cord injuries there are some limitations to this approach. Transplantation of olfactory ensheathing cells from olfactory mucosa significantly improves motor function recovery and reduces the size of cysts[10,11]. However, there is a problem with olfactory ensheathing cell culture heterogeneity because it is currently difficult to purify these cells to a 100% pure culture, so there might be some side effects[12–14]. Mesenchymal stromal cells can also be obtained from olfactory mucosa. As it was mentioned in the manuscript, studies show that mesenchymal stromal cells transplantation has side effects such as neuropathic pain[15]. The use of neurospheres containing neural stem/progenitor cells from olfactory mucosa is associated with difficulties in calculating the number of cells and the percentage of neural stem/progenitor cells in suspension.

Safety of cell-based treatments is a fundamental concern for regenerative medicine. Efficacy is usually the main focus, however, the safety of each treatment is also tested during the trials[16]. Clinical observations show that olfactory ensheathing cell transplantation is safe for patients and there were no serious adverse reactions in all cases[17]. Clinical trials of NSPCs and MSCs from the olfactory mucosa have not been performed to date. The types of cells from the olfactory mucosa are presented in Table 2[18].»

10 Stepanova OV, Voronova AD, Chadin AV, Valikhov MP, Abakumov MA, Reshetov IV, Chekhonin VP. Isolation of Rat Olfactory Ensheathing Cells and Their Use in the Therapy of Posttraumatic Cysts of the Spinal Cord. Bull Exp Biol Med 2018; 165: 132–135. [PMID: 29796806 DOI: 10.1007/s10517-018-4114-x]

11 Voronova AD, Stepanova OV, Chadin AV, Fursa GA, Karsuntseva EK, Valikhov MP, Semkina AS, Reshetov IV, Chekhonin VP. The Effect of Transplantation of Olfactory Ensheathing Cells on the Size of Posttraumatic Spinal Cord Cysts. Bull Exp Biol Med 2021; 171: 122–126. [PMID: 34046791 DOI: 10.1007/s10517-021-05183-7]

12 Reshamwala R, Shah M, Belt L, Ekberg JAK, St John JA. Reliable cell purification and determination of cell purity: crucial aspects of olfactory ensheathing cell transplantation for spinal cord repair. Neural Regen Res 2020; 15: 2016–2026. [PMID: 32394949 DOI: 10.4103/1673-5374.282218]

13 Oieni F, Reshamwala R, St John J. Olfactory Ensheathing Cells for Spinal Cord Injury: The Cellular Superpowers for Nerve Repair. Neuroglia 2022; 3: 139–143. [DOI: 10.3390/neuroglia3040009]

14 Hu X-C, Lu Y-B, Yang Y-N, Kang X-W, Wang Y-G, Ma B, Xing S. Progress in clinical trials of cell transplantation for the treatment of spinal cord injury: how many questions remain unanswered? Neural Regen Res 2021; 16: 405. [DOI: 10.4103/1673-5374.293130]

15 Ichim TE, Solano F, Lara F, Paris E, Ugalde F, Rodriguez J, Minev B, Bogin V, Ramos F, Woods EJ, Murphy MP, Patel AN, Harman RJ, Riordan NH. Feasibility of combination allogeneic stem cell therapy for spinal cord injury: a case report. Int Arch Med 2010; 3: 30. [PMID: 21070647 DOI: 10.1186/1755-7682-3-30]

16 Bartlett RD, Burley S, Ip M, Phillips JB, Choi D. Cell Therapies for Spinal Cord Injury: Trends and Challenges of Current Clinical Trials. Neurosurgery 2020; 87: E456–E472. [PMID: 32497197 DOI: 10.1093/neuros/nyaa149]

17 Cheng Z, Wang R, Cao K, Wang G, Qin J, Li H, Li J, Wang D, He X. Ten years of clinical observation of olfactory ensheathing cell transplantation in patients with spinal cord injury. J Neurorestoratology 2021; 9: 106–116. [DOI: 10.26599/jnr.2021.9040009]

18 Salazar I, Sanchez-Quinteiro P, Barrios AW, López Amado M, Vega JA. Anatomy of the olfactory mucosa. Handb Clin Neurol 2019; 164: 47–65.

2. It may help to enhance logic by briefly introducing the types of olfactory mucosa cells and exogenous neurotrophin therapy before describing them (e.g. using graphics or tables).

We added text and table to the chapter “Introduction”.

“The application of neurotrophins in combination with olfactory mucosa cells can enhance the therapeutic effect of these cells. This combination promotes cell survival, axonal regeneration, structural and functional repair after injury Table 1.”

Round 2

Dear Authors, Thank you for revising the manuscript. I have minors revisions before to accept the manuscript for publication: ----1 Part 3.3 and part 4.4 should be part 3 and part 4. ----2 Figure 1 was already published. If it is necessary, the authors should request the permission to Bull Exp Biol Med Journal to publish again the figure.----3 The references 25 and 27 are repeated, please revise it. -----Please revise in the attached file "80169 Auto_edited" and reply within seven days, thank you!

1.We changed abbreviated words to full ones in the titles of chapters 3 and 4 (“Three – dimensional” instead 3D and “Four-dimensional” instead of 4D) so as not to confuse the numbering of the chapters. 2. We have received and attached permission to publish the Figure 1 again. We have a certified translation of the permission and are ready to provide it to the editors. 3. We corrected the references 25 and 27. Thanks a lot. Best regards, Dr. Stepanova