



Faculty of Medicine  
Department of Anatomy, Cell Biology and  
Physiological Sciences



February 2021

Elie D. Al-Chaer, PhD, JD  
Professor & Chairperson

Marwan El-Sabban, PhD  
Professor & Vice Chair

Wassim Abou-Kheir, PhD  
Associate Professor

Kassem Barada, MD  
Professor

Ali Bazarbachi, MD, PhD  
Professor

Adel E. Birbari, MD  
Professor

Georges Daoud, PhD  
Assistant Professor

Assaad Eid, PhD  
Associate Professor

Abdo Jurjus, PhD  
Professor

Nada B. Lawand, PhD  
Assistant Professor

Fadi Mourad, MD  
Professor

Hala Muhtasib, PhD  
Professor

Rihab Nasr, PhD  
Associate Professor

Dany Nassar, MD, PhD  
Assistant Professor

Makram Obeid, MD  
Assistant Professor

Raya Saab, MD  
Associate Professor

Youssef Zeidan, MD, PhD  
Assistant Professor

Sawsan Zeidan  
Administrative Assistant

Talar Terzian  
Secretary

Manuscript ID: 05863667

Editors-in-Chief, World Journal of Stem Cells

Re: Manuscript Revision

Re: Central Nervous System Tumors and 3D Cell Biology: Current and Future Perspectives in Modeling

Dear Editors-in-Chief,

On behalf of my colleagues, I am returning to **World Journal of Stem Cells** a revised version of a manuscript entitled: “**Central Nervous System Tumors and 3D Cell Biology: Current and Future Perspectives in Modeling**”.

The authors thank the Editors-in-Chief and the reviewer for the constructive suggestions he provided. Those comments are all valuable and very helpful for revising and improving our paper. We have studied and evaluated the comments carefully and have made the amended corrections. We believe that this version has addressed all the raised concerns. Accordingly, we have modified our manuscript to address all these comments. Please find below a point-by-point reply to all comments.

I sincerely hope that this manuscript will meet your requirements for publication.

Sincerely Yours,

Wassim Abou-Kheir, PhD  
Associate Professor  
Department of Anatomy, Cell Biology and Physiological Sciences  
Faculty of Medicine  
American University of Beirut  
Bliss Street, DTS Bldg, Room 116-B  
Beirut, Lebanon, 1107-2020  
Tel: 961-1-350000, Ext. 4778  
Mobile: 961-76994308  
Fax: 961-1-744464  
E-mail: [wa12@aub.edu.lb](mailto:wa12@aub.edu.lb)

Reviewer #1:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Major revision

**Specific Comments to Authors:** This manuscript introduces the development of CNS tumor model preparation and application from the perspective of three-dimensional models, which is of great value. However, the overall logic of the manuscript is not clear, and it fails to intuitively reflect the associations and differences between the 3D-sphere, organoids and brain chip models. In general, although the selected topic of the manuscript is good, there are still many areas that need to be revised. The details are as follows: 1. For the 3D-sphere model, simply summarize a table of CSC biomarkers for readers will be better. 2. It is necessary to supplement the comparison table of 3D-sphere model and organoids so that readers can choose the model in a targeted manner. 3. After the introduction, the common advantages of the 3D model compared to the 2d model should be summarized (such as the content of citations [28-34] in the manuscript) and cited (PMID: 33520358), so as to highlight the value of this review. 4. In addition, in my opinion, the chip model should be distinguished from the organoids. As you show in Figure 1, the 3D-sphere model, organoid and chip model should be the same level of model manufacturing solutions. 5. For each type of model, the manuscript should be divided in more detail. For example, the content could be further divided into modeling technology, application, and limitations, etc... In addition, if possible, I think that appropriate supplementation of the content of cell interaction in the tumor microenvironment may be more helpful to attract readers.

**Response:**

**We thank the reviewer for his/her comprehensive assessment of our manuscript.**

**1. As per the reviewer's comment, for the 3D-sphere model, we have now summarized in a table the CSC biomarkers (Table 2).**

**2. As per the reviewer's comment, we have now added new tables to supplement the comparison of 3D-sphere model and organoids so that readers can choose the model in a targeted manner.**

**3. We have now added Table 1 showing common advantages of the 3D model compared to the 2D model**

**4 and 5. Now we included Table 4 summarizing organoid and organoid-on-a-chip models and Table 3 demonstrating characteristics of 3D modeling technologies.**

**5. We have now included appropriate supplementation of the content of cell interaction in the tumor microenvironment to attract readers.**