

Reviewer #1: This manuscript entitles "Isolation and characterization of mesenchymal stem cells in orthopaedics and the emergence of compact bone mesenchymal stem cells as a promising surgical adjunct" could be considered after revision. 1) The "Abstract section" was missed from the text. Please involve it.

*Thank you for this comment. We have included an abstract.*

2) The manuscript will be more complete if the authors use and involve the articles related to isolation of MSCs from another sources and tissues. For this purpose, you can use and refer the following paper which explained elaborately the Isolation, Immunophenotypic characterization and Multi-lineage differentiation of MSCs derived from heart and liver of zebrafish. It could be better you involved this paper in the "Sourcing of MSCs" or "Characterization techniques" section: } Immunophenotypic characterization, multi-lineage differentiation and aging of zebrafish heart and liver tissue-derived mesenchymal stem cells as a novel approach in stem cell-based therapy. Tissue and Cell. 2019 Apr 1;57: 15-21.

*Thank you for this comment. We have added in a sentence with this important contribution to the manuscript and have included the citation.*

*"MSCs isolated from animal models have consistently demonstrated capacity for multi lineage differentiation, pluripotency, and myriad MSC surface markers"*

3) In the following of above comment, you can use and refer the following paper which discussed the role of stem cells in cell-based therapy and regenerative medicine in the "Clinical applications of MSCs in orthopaedic surgery": } Stem cell-based regenerative medicine. Stem Cell Investigation. 2019;6(19). Doi: 10.21037/sci.2019.06.04.

*Thank you for this comment. We have included this citation in the manuscript and appreciate the important contribution to our work.*

Reviewer #2: The manuscript review of Manuscript ID 56054 and entitled "Compact Bone Mesenchymal Stem Cells in Orthopedic Trauma" by Albert Anastasio et al., is on Mesenchymal Stem Cells sourcing, isolation and characterization techniques and on the potential application of MSC derived from compact bone in orthopaedic trauma. Several concerns and suggestions are listed in major and minor revisions.

Major revisions 1. The title reported in the manuscript is different.

*Thank you for this comment. The correct Manuscript Title is, "Isolation and characterization of mesenchymal stem cells in orthopaedics and the emergence of compact bone mesenchymal stem cells as a promising surgical adjunct." We have made this change.*

2. The English could be revised; some sentences are unclear.

*Thank you for this comment. We have undergone full review of the manuscript, attempting to clarify sentence structure and syntax. We think the manuscript is much improved.*

3. Several references are not correctly cited in the text. Some references not refer to the reported text i.e ref. n. 4 no CB-MS, ref.69 no BM-MS, etc; some authors mentioned in the text not correlated to the author name of the indicated reference i.e. Beaver with ref. n.18, etc; in other cases, the author names cited in the text there are not references. The authors should revise the text and the cited references.

*Thank you for this comment. There does appear to have been an issue with Endnote syncing between computers. We have updated correctly, and the citations should now be accurate.*

4. The authors talk about the CB-MS unique ability to withstand the harsh conditions existing in the recipient tissue. Which are? They could add information in the text.

*Thank you for this comment. We have expanded upon these conditions in the text.*

“The mechanisms behind enhanced survivability in the hypoxic condition are numerous, and may include the enhanced production of a variety of protective cytokines.[22,21] Regardless, post-traumatic inflammation, reactive oxygen species, and compromised blood flow inducing hypoxic tissue state complicate the in vivo environment after fracture, and thus, CB MSCs may be better suited for orthopedic tissue engineering than their bone marrow-derived counterparts.[21]”

5. The figure 1 is not complete. The authors should correct it, add the title and define the acronyms used.

*Thank you for this comment. We have added details to make the text more clear.*

Minor revisions - Table 1: Add the title of the table. - Check “1985” after the ref. 26 in the text. - Describe in the text the muMPC and CFU-GM acronyms. - Correct the form of the reference n. 72 in the text. - Change “pion disease” with “prion disease”. - References of the text, table 1 and figure 1: the formatting is not uniform.

*Thank you for this comment. All minor revisions were corrected.*

Reviewer #3: This review summarized the isolation and characterization of mesenchymal stem cells in orthopaedics and the emergence of compact bone mesenchymal stem cells as a promising surgical adjunct. The paper is well written. However, the mechanisms of MSC on tissue regeneration are not mentioned.

Furthermore, the authors mentioned that compared with BM-MSCs and AD-MSCs, CB-MSCs have superior ability to survive in hypoxic conditions while remaining biosynthetically active. This is very important. However, why? Any cytokines involved in this difference. To my knowledge, IGF-1 is very important in this process (Stem Cell Res Ther. 2020 Jan 9;11(1):22. doi: 10.1186/s13287-019-1544-y.). It is important to include a brief discussion on this topic.

*Thank you for this comment. This is absolutely an important topic to discuss, and we have made sure to include this important reference. We thank you for your assistance.*