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Reviewer A

1) First, the abstract needs some revisions. The rationale for this review was described as "the molecular mechanisms through which CX43 regulates the function and homeostasis of osteoblasts have not yet been elucidated", however, a review, not an empirical study, cannot address this question. The methods need to briefly describe the inclusion criteria for related studies, data extraction, and how the information from the literature was analyzed. The conclusion including the conclusion of the main text need comments for the current

   Response: Thank you for your suggestions. We have revised and improved the presentation in the abstract and introduction section.

2) Second, the introduction of the main text did not explain the clinical needs for this review topic, why an up-to-date review is needed, and why a review could address this research focus.

   Response: Thank you for your suggestions. We add to this section in the introduction to the main text.

3) Third, in the methodology of the main text, the inclusion criteria need to be more detailed; otherwise the inconsistency between the two authors would be substantial.

   Response: Thank you for your suggestions. Detailed literatures inclusion and exclusion criteria are shown in Table 1

4) Fourth, in the discussion of the main text, it seems that the authors rare repeating what the included studies found. However, as a review article, comments on the methodology and limitations of prior studies are needed. In the conclusion part, please have comments on the unaddressed questions and suggest how to solve, to advance the literature.

   Response: Thank you for your suggestions. Relevant content has been added to "Conclusions and future prospects".

5) Finally, please kindly consider to cite several related papers: 1. Huang Y, Liu W, Liu Y, Zhang M, Lv X, Hu K, Xu S, Lu M. Glycated serum albumin decreases connexin 43 phosphorylation in the corpus cavernosum. Transl Androl Urol 2022;11(11):1486-1494. doi: 10.21037/tau-22-317. 2. Yang HT, Li LL, Li SN, Wu JT, Chen K, Song WF, Zhang GB, Ma JF, Fu HX, Cao S, Gao CY, Hu J. MicroRNA-155 inhibition attenuates myocardial infarction-induced connexin 43 degradation in cardiomyocytes by reducing pro-inflammatory macrophage activation. Cardiovasc Diagn Ther 2022;12(3):325-339. doi: 10.21037/cdt-21-743. 3. Yao J, Ke J, Zhou Z, Tan G, Yin Y, Liu M, Chen J, Wu W. Combination of HGF and IGF-1 promotes connexin 43 expression and improves ventricular arrhythmia after myocardial infarction through activating the MAPK/ERK and MAPK/p38

signaling pathways in a rat model. Cardiovasc Diagn Ther 2019;9(4):346-354. doi: 10.21037/cdt.2019.07.12.

Response: Thank you for your suggestions. These papers are of great interest and we have cited them in introduction.

Reviewer B

The paper titled "Connexin 43 in the function and homeostasis of osteocytes: a narrative review" is interesting. Cx43 is expressed in osteoblasts, osteoclasts, and osteoclasts and plays an important role in regulating the function, signal transduction, and mechanotransduction of osteocytes. This review offers a new contribution to the literature by summarizing the relationship between Cx43, a key protein of bone tissue, and osteoblasts. However, there are several minor issues that if addressed would significantly improve the manuscript.

1) What is the new role of mitochondrial Cx43 and hemichannels in modulating mitochondria homeostasis and function in bone osteocytes under oxidative stress? Suggest adding relevant content.

Response: Thank you for your suggestions. Relevant content has been added to "Osteocyte Cx43 and signal transduction".

2) There are many databases. Why did the author only select several databases in this study for searching? Please explain the reason.

Response: Thank you for your suggestions. PubMed, EMBASE, Cochrane Library, and Web of Science are the major databases in medicine, and we also referred to other studies (1、doi:10.1136/bmj.k4226, 2 、 doi:10.1093/eurheartj/ehaa793, 3 、 doi:10.1016/S1473-3099(20)30276-0) to collect literatures as comprehensively as possible.

3) It is recommended to increase the effects of Cx43 on the regulation of osteocyte-to-osteoblast differentiation.

Response: Thank you for your suggestions. Relevant content has been added to "Osteocyte Cx43 and signal transduction".

4) This study is based on the analysis and summary of the literatures. It is suggested to add clinical experimental research, which may be more meaningful.

Response: Thank you for your suggestions. Indeed cx43 has applications in a wide range of cancers (doi.org/10.3390/biom10091240), however the review is more concerned with exploring its mechanisms. In addition, we considered additionally reviewing studies of Cx43 in clinical practice. Thank you again for your suggestions!

5) What are the roles of Cx43 in skeletal aging, estrogen deficiency, and glucocorticoid excess associated bone loss? Suggest adding relevant content.

Response: Thank you for your suggestions. Relevant content has been added to "Osteocyte Cx43 and signal transduction".

6) What is the function and mechanism of Cx43 in other directions? It is recommended to add analysis and comparison.

Response: Thank you for your suggestions. In addition to skeletal diseases, the function and mechanism of Cx43 involve cardiovascular disease, urology, and oncology. Due to space constraints, this section is briefly mentioned in the introduction and conclusion.