

Thank you for all your valuable comments! We invested a lot of effort and utilized the entire granted timespan of two weeks to substantially revise our manuscript. We covered each comment raised and the specific point-by-point response as follows:

Reviewer (code: 02702057)

Q1: Please add the aim of your study in the abstract. Please specify on the text the kind of review you made (systematic, narrative, and so on).

A1: Thank you very much for your valuable comments and suggestions. We have added "This is a narrative review about DAM. We summarize the methods for decellularizing and sterilizing adipose tissue, and the impact of these methods on the biological and physical properties of DAM." to the abstract.

Q2: The authors could be add a graphical abstract to explain in a better fast way the aim and the design of this study and to help better readers understand.

A2: We prepared the 'graphical abstract' as requested. We want to thank the reviewers for this suggestion!

Q3: Please improve the cartilage paragraph and add a sentence regarding the the expression of lubricin and the use of chondropellet of mesenchymal stem cells derived from adipose tissue as an alternative method in tissue regeneration

A3: The comments and suggestions made by the reviewer are very helpful for us to revise the manuscript. In the cartilage paragraph, We add a sentence to explain this phenomenon. 'Adipose-derived mesenchymal stem cells are also used for cartilage regeneration, which differentiates into chondrocytes and can produce important proteins required for articular cartilage (such as Lubricin mucus glycoprotein)'. According to the reviewer's suggestions, the references have been added.

Q4: In the conclusion section please add the clinical relevance of your work.

A4: Thank you for your valuable comments. In the conclusion section, we add the sentence "For DAM, preliminary progress has been made in clinical soft tissue regeneration and metabolic diseases. The combination of DAM with stem cells or growth factors has important indication value in preclinical studies such as wound healing, nerve repair, cartilage and bone tissue engineering and bionic system." to summarize the clinical relevance of DAM.

Reviewer (code: 02566952)

Q1: Whether ECM is ranked the most important?

A1: Thank you very much for your helpful questions. As a niche of stem cells, ECM plays an important role in its proliferation and differentiation. Just as you said, the main component of the niche is ECM, but there are still other important factors (such as biochemical cues physical parameters, various signaling molecules etc.) in the process of stem cell proliferation and differentiation. Therefore, whether it is listed as the most important remains to be further researched.

Q2: Maybe presenting the advantages and disadvantages of supportive scaffolds compared to DAM within a summary table would be of use.

A2: Thank you very much for your insightful suggestions. In this review, we focus on the methods for decellularizing and sterilizing adipose tissue, and the impact of these methods on the biological and physical properties of DAM. The advantages and disadvantages of supportive scaffolds compared to DAM may be the focus of our next review after continuing study to related literature.

Q3: In the literature search chapter I think it would be good to provide the Boolean terms used (if it is the case) and Filters for advanced search would need as well specification.

A3: The comments and suggestions made by the reviewer are very helpful for us to revise the manuscript. We modified the literature search chapter: Literature search was

conducted using the PubMed Advanced Search Builder. Advanced search was performed using ‘decellularized adipose tissue or adipose-derived matrix or acellular adipose matrix or decellularized adipose matrix’ as the title elements, and identified 236 studies. After further analysis and evaluation on whether the title and abstract involve fat-derived ECM and whether the article is written in English, a total of 75 studies were included.

Q4:In the chapter dedicated to assessment of properties of DAM, it would be good to include equipment necessary for mechanical testing and a brief overview of the procedure. Histological and IHC does not offer an insight on the quality of collagen which might be degraded during processing while still present for staining. Staining should maybe belong to a chapter of assessing DAM structure. This chapter should maybe divided in one related to DAM structure – EM, histology IHC and mechanical properties.

A4:We thank the reviewer for this deep insight comment and revised as required. In the Characterization of DAM, We combine the structure and physical properties of DAM in one chapter. A brief overview of the equipment and procedures required for mechanical testing are added. Atomic force microscopy (AFM) can be very useful in detecting the mechanical properties of decellularized tissues. As you said, we added the sentence ‘There is currently no effective detection for the quality of these proteins in DAM.’ to explain the limitation of histological and IHC.

Q5:LIVE/DEAD assay is not based on fluorescein but on polyanionic dye calcein for live cells, and on EthD-1 for dead cells.

A5:We thank the reviewer for pointing out this error and corrected the sentence accordingly. In the paragraph of DAM biocompatibility testing, We added the sentence ‘LIVE/DEAD analysis was performed by staining living and dead cells using a combination of Calcein and EthD-1.’.

Q6:Are there comparative studies between DAM obtained from different sources

(lipectomy versus lipoaspirate for example?)

A6: Thank you for your helpful questions. In my opinion, mechanical treatment whether lipoaspirate or lipectomy has a certain degree of influence on the structure of DAM. We think the damage should be minimal compared to the chemical and biological treatment. According to the current literature, there is no comparative study on DAM obtained from different sources (e.g. lipectomy and lipoaspirate).

Q7: The main author of the article regarding the pilot study in human dorsal wrist implantation is not Lauren but Kokai.

A7: We thank the reviewer for pointing out this error and corrected the sentence accordingly.