

Peer review

The manuscript is well written and well presented. However, it leaves out critical and important content (as referenced and described below). Also, the manuscript does not meet the Journal's expectations for a review paper as seen here: <https://jhss.scholasticahq.com/for-authors>, types of manuscripts, review papers, thus cannot be published as currently written. However, if the author revises the manuscript to include the content left out AND poses (and addresses) the QUESTION below, I will be happy to re-review the manuscript again. The author is requested to perform a thorough search of the literature with regard to the references below; there may be more content that can be extracted from the public domain.

Content left out (see references):

Role of piezoelectric materials, gastrointestinal tract microbiota composition, nerve innervation into regenerated skeletal muscle, self assembling cell sheet engineering, silica nanocomposites, temporal programming of M1 to M2 macrophage transition upon implantation of tissue construct, how the immune system repairs skeletal muscle (GDF3 and others),

QUESTION: Should skeletal muscle tissue constructs also incorporate certain components of the immune system (such as M2 macrophages) so that immunosurveillance mechanisms after implantation are blunted ?

<https://doi.org/10.3390/bioengineering10070800>

<https://doi.org/10.1021/acsbiomaterials.3c01078>

<https://doi.org/10.1007/s10439-024-03541-w>

<https://doi.org/10.3390/ijms25115811>

<http://dx.doi.org/10.1039/C5TB01714A>

<https://doi.org/10.7554/eLife.89381.3.sa0>

<https://doi.org/10.1038/s44319-023-00028-y>

<https://doi.org/10.1093/burnst/tkae013>

<https://doi.org/10.1002/adfm.202308552>

<https://doi.org/10.2147/IJN.S436081>

Gehlert S, Jacko D. The role of the immune system in response to muscle damage. *Dtsch Z Sportmed.* 2019; 70: 242-249. doi:10.5960/dzsm.2019.390

<https://doi.org/10.1016/j.immuni.2016.10.016>

<http://dx.doi.org/10.1152/jappphysiol.00374.2022>

To address "The Role of Piezoelectric materials" in the content left out I added a segment about the role of piezoelectric materials in skeletal muscle tissue engineering in the third section of the paper (the section titled "3.Skeletal Muscle Tissue Engineering")

To address the topic of "Gastrointestinal Tract Microbiota Composition" in the content left out, I added a new section to my paper titled "6. Effects of Gut Microbiome." In this section, I elaborate on the bacterial genera affecting skeletal muscle regeneration, the bacterial metabolites influencing this process, and the overall impact of the gut microbiome on skeletal muscle regeneration. Additionally, I discuss strategies for reducing the numbers of bacterial genera that negatively affect skeletal muscle regeneration without significantly impacting other beneficial bacteria in the gut microbiome.

To address "Nerve Innervation into Regenerated Skeletal Muscle" in the content left out I shortly mentioned the importance of innervation of skeletal muscle in the third section (the section titled "3.

Skeletal Muscle Tissue Engineering”). In the fourth section of the paper (the section titled “4.Common Stem Cell Types Used in Skeletal Muscle Tissue Engineering”) I further elaborated on methods and cells that can be added to increase innervation potential in skeletal muscle tissue constructs

To address “Self Assembling cell Sheet Engineering” in the content left out I added a segment to the end the third section of the paper (the section titled 3.Skeletal Muscle Tissue Engineering”) elaborating on what cell sheet engineering is, the methods used in cell sheet engineering, and its advantages and disadvantages compared to traditional scaffold-utilizing tissue engineering

To address “Silica Nanocomposites” in the content left out I extended the segment where slow-release mechanisms were being covered in the eight (used to be sixth) section of the paper (the section titled “ to also include the use of Silica Nanocomposites for the sustained release of compounds

To address “Temporal Programming of M1 to M2 Macrophage Transition Upon Implantation of Tissue Construct” and “How The Immune System Repairs Skeletal Muscle (GDF3 and others)” in the content left out I added a new seventh section to my paper titled “7.Effects of the Immune System”. In this section, how each phenotype of macrophages contributes to muscle repair, how the factors associated with these macrophages (such as GDF3) contribute to muscle repair, how the transition from the M1 macrophage phenotype to the M2 macrophage phenotype occurs and can be encouraged are all elaborated on.

To address the comment suggesting that I should pose and address the question, “Should skeletal muscle tissue constructs also incorporate certain components of the immune system (such as M2 macrophages) so that immunosurveillance mechanisms after implantation are blunted?”, I included a discussion in the new seventh section, titled “7. Effects of the Immune System”. In this section, I restated the question as, “Should skeletal muscle tissue constructs incorporate certain components of the immune system, such as M2 macrophages, to blunt immunosurveillance mechanisms following transplantation?”, and then addressed it in the following sentences.

Thank you for addressing my comments. Accept.