

Dear editor,

We have fully addressed each concern and hope that this revised manuscript is now acceptable. We have carefully considered the reviewer's comments and worked to include them in the revised version of the manuscript according to the proposed suggestions. Each concern is discussed in detail below. Revisions within the text are marked in red. Thank you for allowing us to resubmit our manuscript for your consideration.

Please find below (in bold) the authors' responses to the reviewer's comments.

Reviewer #1

- Perhaps it would be necessary a reference after the third sentence of the introduction.

The required reference has been added according to the reviewer's suggestion.

- Perhaps authors could comment some comparative studies in which the results with adipocytes and bone marrow stem cells are compared.

We refer here to Ref.13: "the forms of stem cells derived from bone marrow, umbilical cord, or adipose tissue showed no significant differences in terms of morphology, immunogenicity, and pluripotent differentiation". A thorough comparison between the impact of adipose tissue and bone marrow stem cells is the object of a review study (Zhang et al, World J Stem Cells. 2014;6(4):491-6) which has now been added in the introduction section according to the reviewer's suggestion (Ref.14).

Reviewer #2

Has this method been used in the clinic trial?

To our knowledge, the method has not been used in the clinic trial for patients with skin flaps.

In discussion part, on line 4, after "adipose-derived stem" may be added "cells".

The required word has been added according to the reviewer's suggestion.

Reviewer #3

- The authors have organized the manuscript in introduction, discussion and conclusion. I think it would be more appropriate not to include the paragraphs "Effect of ADSCs on viability of random pedicle skin flaps", "Effect of ADSCs on viability of axial pedicle flaps", "Effect of ADSCs on viability of prefabricated pedicle flaps" under the heading discussion because the authors only report and don't discuss the data presented about the topic object of the manuscript. Please modify the manuscript organization.

The manuscript structure has been modified according to the reviewer's suggestion. The title "Discussion" has been omitted.

- In the review there are no images or figures or tables that could facilitate the reading of the manuscript to non-expert. Please add.

The most relevant publications have been summarized in a table, that facilitates the reading of the manuscript.

- I would change the title in "The role of adipose-derived stromal cells in pedicle skin flap survival in experimental animal models"

The title was revised according to the reviewer's suggestion.

-The manuscript is a review or a mini-review? I believe that the mini-review format is better.

We agree with the reviewer's comment that the mini-review format is better.

Reviewer #4

1. The most relevant publications should be summarized in a table.

The table was added according to the reviewer's suggestion.

2. There is no data regarding the animal studies. Data should be mentioned, when available.

Our work reviews only animal models and all available data is mentioned.

3. The conclusion should be shortened and no further studies introduced in it.

The conclusion was revised, containing now no references, according to the reviewer's suggestion.

4. The Keywords should be added: stem cell, skin defect, reconstructive surgery.

The suggested keywords were added according to the reviewer's recommendation.

5. The current state of the research regarding stem cells derived from human skin tissue should be mentioned.

For the current applications of stem cells we refer to Gir et al (Ref.18) in the introduction section. A thorough description is beyond the scope of a mini-review focusing on skin flap survival.

6. further points:

a) Abstract, line 4: Please change to 'most common is necrosis'.

The sentence was revised according to the reviewer's suggestion.

b) Discussion, line 2: Change to 'by Lu et al. in 2008'.

The sentence was revised according to the reviewer's suggestion.

c) Explain the abbreviation ICR mice (mice originating from a Swiss mice strain from Institute for Cancer Research in Philadelphia)

The abbreviation is explained at first mention, according to the reviewer's suggestion.

d) Explain the abbreviation DiI-labeled: chemical used for labeling cell membranes and hydrophobic structures.

The abbreviation is explained at first mention, according to the reviewer's suggestion.

e) Discussion, 2nd page, line 2: Change to 'blood vessel regeneration in vivo'.

The sentence was revised according to the reviewer's suggestion.

Sincerely,

Marios Papadakis

Corresponding author