

RESPONSES TO REVIEWERS



December 05, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6624-review.docx).

Title: The distinction of white, beige and brown adipocytes derived from mesenchymal stem cells

Author: Anna Park, Won Kon Kim, Kwang-Hee Bae

Name of Journal: *World Journal of Stem Cells*

ESPS Manuscript NO: 6624

The manuscript has been improved based on the suggestions of the reviewers:

1. The English language of this manuscript was carefully edited.
2. Revisions were performed based on the suggestions of the reviewers.

(1) Reviewer 1

1. Page 7, line 4: "Some previous evidences supported the idea that BAT development or activity." The sentence lacks the relative references.

➔ We added the references to the amended manuscript.

2. Page 12, line 2: "Until now, many factors that can lead to the browning of WAT have been reported", the authors should also refer to, and comment, a recent paper referring to the overexpression of BMP-4 to promote WAT browning (Qian SW et al. [BMP4-mediated brown fat-like changes in white adipose tissue alter glucose and energy homeostasis](#). Proc

Natl Acad Sci U S A. 2013 Feb 26;110(9):E798-807. doi: 10.1073/pnas.1215236110. Epub 2013 Feb 6. PMID:23388637) that hasn't been considered in the review.

→ As suggested by reviewer, we added this article to the references of the revised manuscript.

3. Page 14, line 2: "Previous studies showed that activated BAT is inversely correlated with BMI, adipose mass and insulin resistance." The sentence lacks the relative references.

→ We added the relevant references to the amended manuscript.

(2) Reviewer 2

The review article by Bae *et al* is concise and fairly comprehensive to a wide range of readers. Though the authors tried to summarize briefly and comprehensively the current knowledge on the adipocyte differentiation into white, brown, and beige adipocytes, they sometimes failed to describe precisely what transcription factors/activators play a role and how these factors work together in beige adipocyte differentiation (mechanistic pathway leading to the beige differentiation).

→ We agree with reviewer's comments. However, the detailed signal transduction mechanism of browning has not been investigated extensively until now. In short, the transcription factors that are involved and how these factors work together in beige differentiation are unclear or unconfirmed, although the involvement of several transcription factors, including PRDM16 and PPAR in beige differentiation has been demonstrated. Therefore, in this review, we omitted a detailed explanation of the signal transduction pathway that induces beige differentiation.

1. There are some typographical errors (or spelling) in the text.

→ We corrected the typographical errors in the amended manuscript.

2. Authors should complete the specific marker (in Table1: it is better to point all the factors known to be specific markers for each type of adipocytes).

→ As suggested, we listed all the known specific markers for each type of adipocyte (see Table 1).

3. It is better to add "activators" section in Table 1 to be more comprehensive.

→ We added an "activator" section to Table 1 of the amended manuscript.

4. Figure 2 is somewhat poor in terms of easy comprehension. It is better to draw an alternative figure to facilitate readers to understand the adipocyte program. To address this, the authors are encouraged to refer to a recent review by Hams and Seale (Nat. Med. 10. 1252-1263, 2013).

➔ We slightly modified Figure 2 to facilitate easy understanding by readers.

Thank you again for publishing our manuscript in the *World Journal of Stem Cells*.

Sincerely,

A handwritten signature in black ink, appearing to read 'Kwang-Hee Bae', with a stylized, cursive script.

Kwang-Hee Bae, PhD

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