

ANSWERING REVIEWERS

December 23, 2013

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 7063-review.doc).

Title: Differentiation of Mesenchymal Stem Cells into Gonad and Adrenal Steroidogenic cells

Author: Takashi Yazawa, Yoshitaka Imamichi, Kaoru Miyamoto, Akihiro Umezawa, Takanobu Tanigushi

Name of Journal: *World Journal of Stem Cells*

PS Manuscript NO: 7063

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated.

2 Revision has been made according to the suggestions of the reviewer

(1) Response to reviewer 00504335

We have corrected the abbreviations, as reviewer suggested (P5-L85, P9-188, P9-198, P10-L203, P12-L269, P13-273).

(2) Response to reviewer 00559125

We have corrected the linguistic problems, as reviewer suggested (P4-72, P8-178~179, P14-L292, P16-L357, Table 2)

(3) Response to reviewer 02446504

(A) Readability would be improved with a definition of what a nuclear receptor is and a table outlining the various nuclear receptors discussed.

We added the description of nuclear receptors (P6-L121~131) and the related references (Mangelsdorf *et al.*, 1995; Robinson-Rechavi *et al.*, 2003). We also added the table (Table 1).

(B) The authors should be clear as to what evidence is derived through in vitro vs in vivo methods.

We re-write the conclusion of *in vitro* experiments (P11-L244~246).

(C) The transplant experiments cited do not explain how transplantation tolerance

is achieved using an apparently allogeneic procedure.

Because MSCs are known to be capable of suppressing immune responses, transplantation tolerance could easily be achievable. They can attenuate the rejection response even in transplantation of other allografts. We added such references (P10-L211~212, Pittenger *et al.*, 1999; Ding *et al.*, 2009).

Specific critiques:

(a) L 72. It is not clear to me that hormone replacement is toxic

We definitely described the side effects and risks in hormone replacement therapy (P4-L79~81)

(b) L186-7. It is not likely that embryonic mesodermal origin is important in understanding differentiation characteristics of MSCs in live born animals

We have changed the sentence (P10-L203~206).

(c) L257. Is SF-1 introduced using plasmids and retroviruses as well?

In LRH-1 experiments, retroviruses were used for introducing both SF-1 and LRH-1. We added this point (P13-L275).

(d) L319. What are parental MSCs?

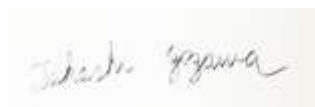
We have changed this point as undifferentiated hBM-MSCs (P15-L337).

(e) L357. Teloeosti: fish?

We have changed this point as teleost fish (P17-L375).

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

Sincerely yours,



Takashi Yazawa, PhD,
Lectures,
Department of Biochemistry
Asahikawa Medical University,
Midorigaoka Higashi 2-1-1-1, Asahikawa, Hokkaido 078-8510, Japan
e-mail: yazawa@asahikawa-med.ac.jp