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January 13, 2014

In Reply Refer To: 691/Research

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Editor
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Dear Editor:

Please find enclosed the edited manuscript in Word format (file name: 6481-Review.doc).

Title: The "Ins" and "Outs" of Mesenchymal Stem Cell Osteogenesis in Regenerative Medicine

Author: Dean T Yamaguchi

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Name of Journal: *World Journal of Stem Cells*

ESPS Manuscript NO: 6481

The author thanks the reviewers for their review of the above manuscript. Revisions to the text are highlighted in yellow.

1. Revision has been made according to the suggestions of the reviewer 00110885
   (1) Figure 1 is added to the manuscript as summary figure. This figure shows Tert transformed cells for self-renewal and their ability to differentiate into various mesenchymal lineages based on substrate (ECM)/scaffold stiffness.
   (2) Table 1a containing recent reviews of clinical trials and case reports are added. Additionally, Table 1b containing two clinical trials and two case reports subsequent to 2008 is also added that were not mentioned in the reviews referenced in Table 1a.
   (3) Additional discussion is given regarding differences in bone marrow-derived mesenchymal stem cells, adipose-derived mesenchymal stem cells, as well as umbilical cord blood and umbilical cord tissue derived mesenchymal stem cells. The differences in their ability to differentiate into osteogenic

versus adipogenic cells based on the type of serum or defined medium used is also given.

(4) Additional discussion is given regarding SDF-1/CXCR4 axis in mesenchymal stem cell migration especially that found in an inflammatory milieu as would be expected in tissue (e.g. bone) injury and the cell sources of SDF-1 that can stimulate mesenchymal stem cell migration.

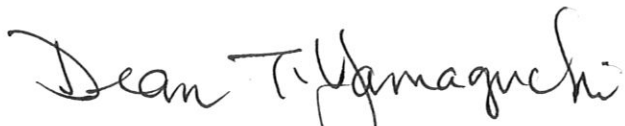
(5) Other CXC and CC chemokines that could potentially play a role in mesenchymal stem cell migration and angiogenesis are also briefly discussed.

(6) Discussion regarding how the stromal/vascular fraction of white adipose tissue that contains mesenchymal stem cells can enhance the growth of already established tumors is also discussed as well as the increase in adipose-derived mesenchymal stem cells that may be present in obesity that could contribute to enhanced tumor growth and tumor vascularity.

2. References have been reformatted according to guidelines.

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

Sincerely yours,



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