Reviewer's report

Title: Higher BMP/smad sensitivity of tendon-derived stem cells (TDSCs) isolated from the collagenase-induced tendon injury model - Possible mechanism for their altered fate in vitro

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Reviewer: Eijiro Maeda

Reviewer's report:

General comment
The submitted manuscript investigated the responsiveness of tendon-derived stem cells (TDSCs) obtained from healthy and collagenase-induced injured patellar tendons in rats to BMP-2 stimulation. The question was clear that was tested using established methods. Although overall the study was designed and conducted well and the manuscript was well written, the impact of the findings obtained is not very high. This is mainly because that the group of authors already showed in their previous studies that BMP-2 induces chondro-osteogenic differentiation of TDSCs, and thus, the present findings just provide one possible pathway of such differentiation, leaving a fundamental question why TDSCs from collagenase-induced injury tendons have different responsiveness from those from healthy tendons unknown. Along with specific comments listed below, the authors may need to address to answer the question, to provide readers of the journal with an interesting insight of the etiology of tendinopathy.

- Major Compulsory Revisions

Methods
1. Page 10, Line 178. “Quantitative and semi-quantitative data was shown in boxplots.” Certainly, the authors used boxplots in Figures 1, 3 and 4, but the style of boxplots used in Figures 1 and 3 and that in Figure 4 seems different. In Figures 1 and 3, the maximum value, the minimum value, first and third quartiles, and median value were provided, while in Figure 4 plots are seemed just to proved the maximum and minimum values and median (mean?) value. In addition, there were error bars for x-axis in Figure 4 without any clear comments or explanation. Therefore, the authors must be consistent in using boxplots.

2. Page 10, Line 182. The use of ANOVA for repeated measures may not be appropriate in this case, as the authors did not measure the same samples at different time points. Please consult it to a statistician.

3. Page 10, Line 183. Statistical significance should be p < 0.05, but not p # 0.05. Please rewrite Results section, Figure legends and Figures using a p < 0.05 criterion.

Discussion
1. Page 14, Lines 258-259; Page 7, Lines 45-46. “Results from this study open the door for human studies of the pathogenesis of tendinopathy.” It is not clear why and how the findings in the present study, using a rat model, are related to human studies. The authors need to rewrite Conclusion as well as Conclusions in Abstract to be more precise.

Figures
1. Page 21, Line 374. Please provide the definitions of outlier and extreme value. Were these values included in statistical analysis?

- Minor Essential Revisions

Background
1. Page 3, Lines 53-56. The sentence “It is characterized by … activity-related tendon pain.” is too long and unclear. Please divide it into 2 or 3 sentences to make it clear, and provide references to each of the characteristics.
2. Page 3, Lines 56-57. “As a result, … with limited success.” Please provide references.
3. Page 4, Line 61 to Page 5, Line 77. In this paragraph, the authors described past studies using animal models, although it is not clear which animal models were used in these past studies.

Methods
4. Page 5, Lines 94-95. Please provide more information on the isolation of TDSCs, at least a brief explanation of the isolation procedures.
5. Page 5, Line 95 to Page 6, Line 98. Please provide the name(s) of stem cell markers examined.

Discussion

Table
7. Page 21, Line 368. Table legend “Table showing the primer sequence, …” should be “The primer sequence, …”.

Figures
8. Page 27, Figure 5. Please provide the names for the column and line, so that readers can easily understand which photograph shows which condition.

Minor issues not for publication
9. Page 1, Line 1, Title. “BMP/sm3 sensitivity …” is “BMP/Smad sensitivity …”?
11. Page 6, Line 105. “… Carlsbad, USA).at 37°C …” should be “… Carlsbad, USA) at 37°C …”.

Abstract

1. Page 2, Lines 34-36. Methods. Indicate which animal model was used.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.