Reviewer’s report

Title: WIF1 enhanced dentinogenic differentiation in stem cells from apical papilla

Version: 1 Date: 27 Jun 2018

Reviewer: Shaomian Yao

Reviewer's report:

This manuscript reports expression of Wnt inhibitory factor 1 (WIF1) in Stem cells from apical papilla (SCAPs) and its role in dentinogenesis of SCAPs by overexpression of the gene. In vitro and in vivo experiments were performed. The results are of interest for the field. The manuscript needs major revision for publication. Specific comments are as follows:

Abstract:
Lines 17-19: Revise the sentence. "---to investigate the function of WIF1 for ---"

Lines 22-32: Methods of the abstract is incomplete.

Methods:
Lines 39-42: This paragraph is redundant as the information are provided in the next paragraph regarding human subjects.

Under "Alkaline Phosphatase and Alizarin Red Detection". The authors described " The final calcium level in each group was normalized to the total protein concentration -------" . There is no description about protein collection and quantification in the Methods. Please provide the description.

Under "Transplantation in nud mice". Was any treatment to induce dentinogenesis applied after transplantation? If not, how could the SCAPs spontaneously undergo dentinogenesis after transplantation? Did the cells undergo other types of differentiation after transplantation?

Results and Discussion:
Fig 1B: What means 0W (0 week)? Does it mean the control without subjecting to differentiation induction? The method for the in vitro experiment of dentinogenic differentiation should be provided in the Methods Section.

Under "WIF1 enhanced dentinogenic differentiation potential of SCAPs in vitro". The Authors state "---the expression of RUNX2 was not significantly different (data not shown)". It would be interested to present the RUNX2 data as it is as important gene in stem cell differentiation. This results of no significant change (SCAP-vector vs SCAP-WIF1) should be discussed.

Fig 4. More specific bone/dentin staining other than H&E would strengthen the result.
Fig 4C. The difference in immunohistochemistry staining of DSPP is not very obvious. A negative control staining without primary antibody should be included to make sure no non-specific staining present.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Unable to assess

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If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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Acceptable

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