



PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 58174

Title: New Insight into Dental Epithelial Stem Cells: Identification, Regulation, and Function in Tooth Homeostasis and Repair

Reviewer's code: 02521831

Position: Peer Reviewer

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: Switzerland

Author's Country/Territory: China

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Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-07-17 12:53

Reviewer performed review: 2020-07-17 15:10

Review time: 2 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

SPECIFIC COMMENTS TO AUTHORS

The review presents a comprehensive discussion of the main aspect of incisors DESCs biology. The information is given in a somehow too synthetic way - the authors wished to discuss many topics in a brief text, and at times the review sounds like a list of results rather than an organic text. The text contains some imprecise or wrong statements. Overall, the fluidity and interconnection of the paragraphs could be significantly improved. "Tooth enamel, one of the most highly mineralized tissues in the human body," - enamel is the highest mineralized tissue of the body "Fully formed enamel has been detected on polyglycolic acid fiber mesh using dissociated porcine third molar tooth germ cells, suggesting tissue engineering as an alternative strategy to regenerate enamel [9]." - the reference for such a big statement is actually wrong. To date, no evidence of synthetic enamel equivalent to the natural one has been provided. "Klein lab has identified dental epithelial stem cells (DESCs) at the proximal end of mouse incisor, in a structure named as labial cervical loop (laCL)." The first report of the cervical loop as DESC was provided not by the Klein Lab, but by Harada et al. 1999 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2164976/>). The language requires extensive editing; in some situations, it is not possible to understand the meaning of the sentence. E.g. "General stem cell marker Lgr5 is knocked into a bicistronic message to detect actual stemness in recent years. The expression of Lgr5 is identified as actively cycling stem cells in the SR of cervical loop epithelium,". The authors should clarify better the difference between the classical model and the newly proposed model of cervical loop cellular organization. "While the differentiation of SI cells was inhibited when the Jagged1 antibody was neutralized," - Jagged1 was neutralized, not its antibody. "Hox is another target gene of Bmi1,". Hox is not a single gene, it indicates a family of genes. "Conditional overexpression of Lef-1 in dental epithelium increased cell



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proliferation and created a new stem cell compartment in the laCL." - is this activity of Lef-1 Wnt-independent? The authors stated before that Wnt is not active in the cervical loop "MiRNAs have a specific function in a distinct compartment of CL because their expression of miRNAs in the liCL, the laCL and the ameloblasts are different through microarray analysis" This sentence is not clear "It is thought that stem cells resided in OEE generate TA cells and SI cells of IEE, which include actively proliferative cells and these cells migrate toward the incisal tip, differentiate to pre-ameloblasts, then to functional ameloblasts, which are responsible for enamel formation [18,39]. A recent study reported a new renewal model in which active-cycling IEE cells give rise to both the functional ameloblasts and the surrounding non-ameloblast epithelial cell populations. There seemed only one cell population, the dividing cells of the IEE, which go through self-renewal during homeostasis [17,18]." This section in paragraph 3.1 is really a repetition of what said at the beginning, when discussing the models. "It has been reported that human tooth germ stem cells could differentiate into epithelial cell types, but not functional cells" Do the authors mean "functional dental epithelial cells"? The implications for enamel regeneration in humans - and the strong limitations - should be more precisely addressed. Figure 2 is not really clear; the authors should propose an alternative visualization



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Title: New Insight into Dental Epithelial Stem Cells: Identification, Regulation, and Function in Tooth Homeostasis and Repair

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Position: Editorial Board

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Professional title: Research Associate

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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SPECIFIC COMMENTS TO AUTHORS

The authors Gan et al. in the following review article entitled: “New Insight into Dental Epithelial Stem Cells: Identification, Regulation, and Function in Tooth Homeostasis and Repair”, clearly describe the current knowledge about the niche of dental epithelial stem cells (DESC) of the rodent incisor that generate enamel-producing ameloblasts and other supporting dental epithelial lineages in homeostasis and injury repair during rodent life span cycle. The authors also report a study about the rare formation of human ameloblasts, enamel and enamel-dentin tissue for a potential therapeutic use in human tooth regeneration and tissue engineering. Further progress is needed in this regard.

Evaluation of the manuscript

1. Title. The title reflects the main subject of the manuscript.
2. Abstract. The abstract summarizes and reflects the work described in the manuscript.
3. Key words. The key words reflect the focus of the manuscript.
4. Background. The manuscript adequately described the background, present status and significance of the study.
5. Discussion. The manuscript interprets the findings adequately and appropriately, highlighting the key points concisely, clearly and logically.
6. Minor revision in point 6. Illustrations. The figures 1 and 2 are of good quality and appropriately illustrative of the paper contents, but figure 3 requires a better legend for understanding the differences of the mouse incisor during homeostasis and injury repair. Authors are requested to clarify it in the legend of figure 3.
7. References. The manuscript cites appropriately the latest, important and authoritative references in the introduction and discussion sections.
8. Quality of manuscript organization and presentation. The manuscript is well, concisely and coherently organized and presented. The English language and grammar is accurate and appropriate. The manuscript is well written and satisfies all criteria for the publication on World Journal of Stem Cells, except for a minor revision in point 6. Thus, I endorse the publication of the



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manuscript with minor revisions in WJSC.