

Reviewers reply for article no 57854 entitled 'Perspectives of pluripotent stem cells in livestock'

ROUND1

Reviewer #1:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors:

This manuscript summarized the current achievements in derivation of PSCs from farm animals and discussed the potential applications. While there are still some key references missed and these advances of research area is important in pluripotent stem cell research.

The comments are as follow: Major concern:

1. Pluripotent stem cell generation by reprogramming germline stem cells such as spermatogonial stem cell and female germline stem cell, the author should contain these references related research in the text, these references are:

1) Guan K, Nayernia K, Maier LS, Wagner S, Dressel R, Lee JH, Nolte J, Wolf F, Li M, Engel W, Hasenfuss G. Pluripotency of spermatogonial stem cells from adult mouse testis. *Nature* 2006; 440:1199–1203.

2) Kanatsu-Shinohara M, Inoue K, Lee J, Yoshimoto M, Ogonuki N, Miki H, Baba S, Kato T, Kazuki Y, Toyokuni S, Toyoshima M, Niwa O, et al. Generation of pluripotent stem cells from neonatal mouse testis. *Cell* 2004; 119:1001–1012.

3) Ko K, Tapia N, Wu G, Kim JB, Bravo MJ, Sasse P, Glaser T, Ruau D, Han DW, Greber B, Hausdorfer K, Sebastiano V, et al. Induction of pluripotency in adult unipotent germline stem cells. *Cell Stem Cell* 2009; 5:87–96

4) Wang H, Jiang M, Bi H, Chen X, He L, Li X, Wu J. Conversion of female germline stem cells from neonatal and prepubertal mice into pluripotent stem cells. *J Mol Cell Biol* 2014; 6:164–171.

5) Lee SW, Wu G, Choi NY, Lee HJ, Bang JS, Lee Y, Lee M, Ko K, Schöler HR, Ko K. Self-Reprogramming of Spermatogonial Stem Cells into Pluripotent

Stem Cells without Microenvironment of Feeder Cells. Mol Cells. 2018 Jul 31;41(7):631-638. 2.

Reprogramming and transdifferentiation are the two mainly aspects in stem cell related research, so the author should at least discuss their relationship as the reference suggested

Jingjing Guo 1, Hu Wang, Xingchang Hu. Reprogramming and transdifferentiation shift the landscape of regenerative medicine. DNA Cell Biol 2013 Oct;32(10):565-72. doi: 10.1089/dna.2013.2104. Epub 2013 Aug 9.

Answer: Content incorporated in the text of manuscript with reference as suggested by reviewer

3. Haploid stem cell is hot in the field of stem cell research at present

Cui T, Li Z, Zhou Q, Li W. Current advances in haploid stem cells. Protein Cell. 2020 Jan;11(1):23-33. doi: 10.1007/s13238-019-0625-0. Epub 2019 Apr 19

it may provide a new resource to generate transgenic modified animal models, therefore, it also need to be carefully addressed in the manuscript.

Answer: Incorporated in the text of manuscript with reference as suggested by reviewer

4. The author mentioned germ cell generation by pluripotent stem cells, there are many different originated stem cell-related germ cell protocol for in-vitro derivation strategy, the reference

Zeng F, Huang F, Guo J, Hu X, Liu C, Wang H. Emerging methods to generate artificial germ cells from stem cells. Biol Reprod. 2015 Apr;92(4):89.

Answer: Suggested reference incorporated with description in the text of manuscript

5. The author should add some ethical concerns about chimeric research that we may need to address or pay attention in the near future of biological research in the text.

Answer: Incorporated in the chimera formation section of the manuscript

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors:

Authors reported well written narrative review article in which livestock of iPS cells is widely considered. The article is logically structured and novel information is given in clear and concise manner. The strengths of the paper are high clarity and well-designed figures that are very attractive for readers and the paper will be cited. The weakness is narrative manner of the paper. Methodological aspects of reproduction, cultivation, harvesting etc are described comprehensive.

Answer: Thank you for your encouraging reports

The plagiarism was not detected.

Answer: Noted with Thanks

The conclusive part is powerful to understand current challenging and perspectives in the future.

Answer: Noted with Thanks

Major concerns: None Minor concerns:

Some grammar errors (contributed instead contributed to etc.) and typos. Please, check and correct them

Answer: checked and corrected

Genom editing tool can be reported in separate subparagraph with unique title.

Answer: Thanks for suggestion and our submission is that description on genome editing in separate subparagraph with title is beyond the scope of this review, although required information on genome editing related to topic has already been presented with sufficient references and that would help readers to get updated information on the topic.

Editorial office's comments: Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor:

1 Scientific quality: The manuscript describes a review of the perspectives of pluripotent stem cells in livestock. The topic is within the scope of the WJSC.

(1) Classification: Grade C and Grade D;

(2) Summary of the Peer-Review Report: This article is logically structured and novel information is given in clear and concise manner. The conclusive part is powerful to understand current challenging and perspectives in the future.

Answer: Thank you for your encouraging reports

However, this manuscript still has some key references missed and these advances of research area are important in pluripotent stem cell research.

Answer: Suggestions incorporated

Reviewer suggest reprogramming and transdifferentiation are the two mainly aspects in stem cell related research, so the author should at least discuss their relationship as the reference suggested; and

Answer: Suggestions incorporated

(3) Format:

1. There are 2 tables and 4 figures. A total of 276 references are cited, including 57 references published in the last 3 years. There are 10 self-citations.

Answer: Noted with Thanks

2 Language evaluation: Classification: Grade B and Grade B. A language editing certificate issued by ICAR was provided.

Answer: No action required

3 Academic norms and rules: The authors provided the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. No academic misconduct was found in the CrossCheck detection and Bing search.

Answer: No action required

The highest single-source similarity index in the CrossCheck report showed to be 11%. The CrossCheck results showed the similarity to be high. According to our policy, the overall similarity index should be less than 30%, and the single-source similarity should be less than 5%. Please rephrase these repeated sentences.

Answer: Needful done

4 Supplementary comments: This is an invited manuscript. The topic has not previously been published in the WJSC. The corresponding author has 1 published articles in the BPG.

Answer: No action required

5 Issues raised: I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

Answer: Original figures in PPT format attached

6 Re-Review: Required.

Answer: Needful done

7 Recommendation: Conditionally accepted.

Answer: Noted with Thanks

ROUND2

Reviewer #1:

Although the author revised a lot based on the reviewer's comments, there are still have some concerns need to be further revised, we need summarize the exact information to the readers. Here is the concern below: Although the author adds germline stem cell derived pluripotent stem cell related development in the text, some of the words used are not accurate based on the knowledge from reviewer at present. As we know, germline stem cell is a class of unipotent stem cell reside in the gonad (testis and ovary), in normal environment, these kind of tissue stem cell only can differentiate into germ cell, based on the gene expression profiling from these two types of tissue stem cell, we can clearly see these two types of are unipotent. While germline lineage makes them, little difference compared with other tissue reside stem cell, they can expand in vitro and converted from unipotent to pluripotent state just under specific culture conditions. Therefore, the author should clearly present SSC and FGSC as well are two unipotent stem cells, and we can manually convert these two unipotent stem cells into pluripotent stem cell in vitro under specific condition. This conversion strategy was used to generate pluripotent stem cell like the iPSC generation, but not for the infertility treatment. Therefore, the author should revise them.

Yes I agree with reviewer comments and accordingly paragraph in the manuscript text has been revised.