

September 03, 2014



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: Final draft (after review)).

Title: Cell signaling pathways underlying induced pluripotent stem cell reprogramming

Authors: Kate Hawkins, Shona Joy and Tristan McKay

Name of Journal: *World Journal of Stem Cells*

ESPS Manuscript NO: 12731

The manuscript has been improved according to the suggestions of reviewers:

1) In the page 9, line 17, there is an error in writing. I guess that the sentence ‘STAT3 signalling was shown to directly block the action the DNA methyltransferase inhibitor DNMT1...’ should be changed to ‘STAT3 signalling was shown to directly block the action the DNA methyltransferase DNMT1...’ by deleting the word ‘inhibitor.’

We have now deleted the word ‘inhibitor’ from page 9, line 17.

2) In the Table 1, small molecules that enhance iPS cell reprogramming are listed. This is surely important information, however, in order to consider the signaling pathway and transcription network, a catalog of the reprogramming factors themselves should be shown as well. It will provide much beneficial insight.

We have added a new Table 1 cataloguing the reprogramming factors mentioned in the manuscript. We have also amended the text to reference this figure (page 4, line 23).

3) As for the Figure 1, the authors should depict the schema of reprogramming pathways separately in the case of mouse and human iPS cells. In this regard, it is informative to describe the similarity and difference between mouse and human iPS cells.

We have now separated Figure 1 into human and mouse.

In addition, it is helpful for readers to show the relationship between the core circuitry of transcription factors (Oct4, Sox2, Nanog) and signaling pathways in pluripotent stem cells in another figure.

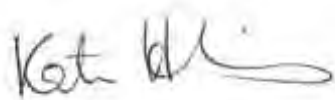
We have added a new Figure (Figure 2) linking the signalling pathways and core circuitry of transcription factors involved in pluripotency. We have also amended the text to reference this figure (page 10, line 26).

Also, it is confusing what ‘gene promoter’ means in the Maturation image. Is it a part of the sentence ‘Demethylation of Pluripotency gene promoters’? If so, the authors should change the form to an easily understood manner.

We have now removed the gap between ‘pluripotency’ and ‘gene promoters’ in Figure 2 so that the sentence ‘demethylation of pluripotency gene promoters’ reads more clearly.

We hope you find our manuscript suitable for publication in the *World Journal of Stem Cells*.

Best regards,

A handwritten signature in dark ink, appearing to read 'Kate Hawkins', with a stylized flourish at the end.

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