



Laboratory of Stem Cell Biology
Kitasato University School of Science

World Journal of Stem Cells
Editorial Office

June 8, 2016

Dear Dr. Lian-Sheng Ma:

Here we are submitting our revised manuscript entitled: “Reprogramming of germ cells into pluripotency (ESPS Manuscript NO: 02270828)” as a review article to *World Journal of Stem Cells*.

We are pleased to read that reviewers have found our review interesting. We revised our manuscript following the reviewers’ comments. On the following pages, we provided point-to-point responses to these comments.

The rewritten parts of the manuscript are highlighted in red and the manuscript had been corrected by native English editors. We are confident that we properly modified the paper as a final version and we hope it will now be suitable for publication in *World Journal of Stem Cells*.

Sincerely yours,

Tohru Kimura

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We would like to sincerely thank the reviewers for their encouraging and constructive comments, and have used these as the basis for revising the manuscript. Here we address the reviewer's comments and our responses.

Reviewer 02446204:

Comments to authors

This review is well written, compactly illustrating the molecular events involved in the regulation of pluripotency, differentiation and tumorigenesis in germ lineage cells. Also, authors' English skills are very high throughout the manuscript. Nevertheless, there are some minor concerns. Before publication in World Journal of Stem Cells, they should be corrected.

Minor concerns:

1. *In page 6, line 11, "in the presence of LF," should be corrected as "in the presence of LIF,,*

We corrected "LF" to "LIF" (line 116 in revised manuscript).

2. *In page 13, line 16, the words "mouse MEFs" sound rather bizarre because "M" in "MEF" means mouse.*

"mouse MEFs" was corrected to "MEFs" (line 283 in revised manuscript).

3. *It seems that the description of gene/protein names lacks uniformity. For example, both "SCF" and "KITLG" were used in the manuscript. Also, gene names were rewritten in italics in some sentences and non-italics in other sentences. Those terms should be used in a constant and standard manner throughout the manuscript.*

We used KITLG throughout the manuscript (lines 100-101, 108, and so on). We also carefully checked and corrected the manuscript so that gene and protein names are written in italics and in non-italics, respectively.

Reviewer 01236209:

Comments to authors

The manuscript summarized the recent progress in reprogramming PGCs into the

pluripotent state. The authors described the key signaling pathways for PGC reprogramming, and compared to their roles in somatic cell reprogramming. In general, this review covers an interesting topic in the stem cell field, and is well written.

I only have a few minor comments:

(1) *Gene names have to be italic.*

We carefully checked and corrected the manuscript so that gene and protein names are written in italics and in non-italics, respectively.

(2) *Add references to Line 22-33, and Line 43-48.*

References to lines 22-33 and lines 43-48 in original manuscript (lines 28-39 and lines 49-54 in revised manuscript) are cited in review references 2 and 3. The two reviews are cited just before these sentences, i.e., in lines 22 and 43 in original manuscript (lines 28 and 49 in revised manuscript). And as last reviewer 02446280 has advised us to shorten the number of references, we did not add further references here.

(3) *Some typos: Line 110 “LF”; Line 163 “(mGCSs)”.*

“LF” and “(mGCSs)” were corrected to “LIF” and “(mGSCs)”, respectively (lines 116 and 169 in revised manuscript).

(4) *Line 236, is “TPR53” correct?*

We corrected “TPR53” to “TRP53” (line 242 in revised manuscript).

Reviewer 01237968:

Comments to authors

In this review manuscript, the authors nicely summarized current knowledge concerning molecular mechanisms underlying reprogramming of germ cells and of somatic cells into pluripotential stem cells and their possible relationship. The information in this manuscript should be valuable for researches in the fields of gem cells biology as well as of stem cell biology, and therefore, it is suitable for publication in this journal.

Reviewer 02446280:

Comments to authors

The paper entitled Reprogramming of germ cells into pluripotency highlights some aspects of germ cells differentiation pathways and re-directioning of these pathways to pluripotency. The review is rather comprehensive although slightly overloaded with examples and references. I would advise to shorten the number of references to the most recent and important to the field.

Following to reviewer's advice, we shortened the number of references from 105 to 91.