

March, 30, 2013

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Dear Dr. Jin-Lei Wang,

Thank you for your email of March 20.

I am happy to learn majority of the reviewers recommended accepting my Editorial entitled: "Cell transplantation therapy using pluripotent stem cells" for publication in World Journal of Immunology.

In accordance with the reviewers comments, the following changes have been made in the original manuscript:

1. The edited manuscript is written in Word format (file name: 2571-Letter FINAL.doc).
2. **Title:** Cell transplantation therapy using pluripotent stem cells
3. **Author:** Noah Isakov
4. **Name of Journal:** *World Journal of Immunology*
5. **ESPS Manuscript NO:** 2571
6. The manuscript has been improved according to the suggestions of reviewers:

Reviewer No. 00503085

This minireview summarized the main discoveries of the recently Nobel prize laureates Prof. Gurdon and Yamanaka. The minireview may be interesting for a general audience but, in my opinion, does not have a direct relation to immunology. There are several papers dealing with the immunogenicity of iPS cells that probably would be more interesting for immunologists. In addition, this topic is controversial and could be discussed.

Answer: I agree with the Reviewer that the manuscript does not directly relate to Immunology. On the other hand, an Editorial on the most recent Nobel Prize in Physiology and Medicine should always be welcome in just any Medical/Biomedical Journal, irrespective of the Journal's specific field.

The issue of iPS cell's immunogenicity is relevant to allogeneic but not autologous cells. Discussions on such specific issues can be included in comprehensive Review articles but not in short Editorials.

As for controversial issues relevant to the future potential use of iPS cells in the clinic, my personal feeling is that their inclusion in this Editorial may diminish the importance of the discoveries that led to the Nobel Prize, something that I personally would not dare to do. Furthermore, this suggestion is in complete contradiction to the suggestion of Reviewer No. 00503085 (see above).

Reviewer No. 00503126

Dr. Isakov has summarized the work that led to the awarding of the Nobel Prize in Physiology or Medicine in 2012. This is an excellent overview of the history of the work. However, the last paragraph appears to minimize the significance of the discoveries by leading with a statement that this work has not led to a useful clinical product. Many concepts discovered by Nobel laureates have not led to clinical products, but remain highly important for our understanding of biology. A broader discussion of how these discoveries contribute to our understanding of biology would be warranted. If Dr. Isakov would like to emphasize the clinical relevance, he could refer to preclinical trials that have shown reason for hope.

Answer: I thank the Reviewer for his/hers constructive comment. In accordance, I have modified the discussion at the end of the Editorial to reemphasize the importance of the discoveries and their potential relevance to the understanding of basic biological questions.

Reviewer No. 00502958

In this editorial, "Noah Isakov" summarizes the research and the major discoveries in the field of cell transplantation therapy using pluripotent stem cells. Globally the editorial is well presented and pleasant. I just have a few minor remarks/corrections. -P1, section 4, line 26: from a mature intestinal cell. Please mention the origin of this cell. -P2, section 1, line 10: Please correct sever in severe. -P2, section 2, line 15: Please correct Cat in cat. -P2, section 2, line 15: Please correct, and ferrets. -Has it not been tried in other species such as dogs, cows, and pigs? -P2, section 4, line 35: Please provide the full names for the four genes, then, use the abbreviations. -In vitro, in vivo, and other Latin words should be in italic.

Answer: I thank the Reviewer for his/hers constructive comments. In agreement, all the suggested changes were introduced into the revised version of the manuscript.

Reviewer No. 00502976

This Editorial concerns the discovery of induced pluripotent stem cells and their potential interest for basic research and clinical application. The manuscript can be published in WJI

Answer: I thank the Reviewer for his/hers recommendation to accept the Editorial in its present form.

Reviewer No. 00503077

It is very good mimi-review of pioneering works of mature cell de-differentiation and reprogramming. I suppose it should be publish without revision

Answer: I thank the Reviewer for his/hers recommendation to accept the Editorial in its present form.

Reviewer No. 00070944

This manuscript is well written and addresses important issue on the potential use of stem cells in treating diverse disorders. I recommend it without any other comments

Answer: I thank the Reviewer for his/hers recommendation to accept the Editorial in its present form.

Reviewer No. 00502940

This is a short and concise review and comments for the application of stem cell therapy, particularly in the historical view. If the author could add a paragraph with a summary table to depict current accomplishments in neuron, heart, and autoimmune disorders, this article would be more favorable for publication.

Answer: I thank the Reviewer for his/hers comment. The focus of the present Editorial is to focus on the breakthrough discoveries of the two Nobel Laureates, which led to revolution in the field of stem cells research, and eventually to winning the Nobel Prize.

My personal feeling is that a summary table that includes the accomplishments of iPS cell usage in neurons, heart, and autoimmune disorders should be part of a comprehensive manuscript that reviews the entire field, rather than a short and focused Editorial.

The format of the manuscript has been updated.

References and typesetting were corrected.

Thank you very much for publishing my manuscript in the *World Journal of Immunology*.

Sincerely,



Noah Isakov