

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

ESPS manuscript NO: 25786

Title: Therapeutic potential of human embryonic stem cells in type-2 diabetes mellitus

Reviewer's code: 00505755

Reviewer's country: Japan

Science editor: Xue-Mei Gong

Date sent for review: 2016-03-23 16:41

Date reviewed: 2016-03-24 16:24

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

General comments (1) The importance of the research and the significance of the research findings This research is important in terms of reporting the result of clinical research using human embryonic stem cells. (2) The novelty and innovative nature of the research This is an innovative research describing about possibility of human embryonic stem cells in type-2 diabetes mellitus. (3) The quality of the manuscript's presentation and readability It is well written, however, the content of the article may be appropriate for clinical category such as Case Report or Clinical Trials study, etc. other than Basic study. (4) The ethics-related aspects of the research Numbers of informed consent documents and patients in the manuscript does not match. Please confirm the informed consent. Specific comments Title: It accurately reflects the major topic and contents of the study. Abstract: It appropriately describes about the content of the manuscript. Introduction: There are some characters that are not shown appropriately. Please correct them in overall manuscript. Materials and Methods: Protocol and patient selection criteria should be explained more in detail. Results: Please explain the meaning of gm% for HbA1c levels. References: Please check reference citations carefully. Figure and Table: The real numbers showing the improvement in each patient should be indicated.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

ESPS manuscript NO: 25786

Title: Therapeutic potential of human embryonic stem cells in type-2 diabetes mellitus

Reviewer's code: 02446204

Reviewer's country: Japan

Science editor: Xue-Mei Gong

Date sent for review: 2016-03-23 16:41

Date reviewed: 2016-03-24 18:13

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input checked="" type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This research article is excellently written. This work has been performed as an advance step for the previous case studies by Dr. Shroff G (J Diabetes Mellitus 5, 313-318, 2015). The current report will make a great contribution to the promotion of the hESC-based regenerative medicine in the field of Diabetes. However, there are several issues to be addressed before publication in World Journal of Stem Cells. I do hope that the author would appropriately revise the manuscript for readers in broad fields. Points to be addressed Materials and Methods 1) In page 8, lines 4-5, the sentence "... so that to allow the recipient's immune system to be active, ..." seems rather confusive for non-expert readers. The aim of the intramuscular administration of smaller numbers of hESCs is to induce immune tolerance, rather than to provoke active immune reactions. Therefore, it would be better to rewrite the sentence as "... so as to induce immune tolerance against hESCs, ..." and so on. 2) In page 8, line 6, the description "... via intravenous (i.v) route to "home in" the required area ..." lacks concreteness. Actually, it is a copy of the sentence in the previous report (Shroff G, J Diabetes Mellitus 5, 313-318, 2015), which also lacks the concrete description regarding the procedure. For readers to correctly understand the work, the detailed transplantation procedure should be written. For

example, readers cannot understand which vein (portal vein or splenic vein?) or which artery (dorsal pancreatic artery or inferior pancreaticoduodenal artery or others?) was used as a route for transplantation. Results: 1) Author should describe the effects of hESC-based transplantation therapy on the incidence of hypoglycemia by summarizing the results in a Table. I think that it is highly possible that the therapy effectively reduced the incidence of hypoglycemia. Discussion: 1) In page 11, lines 7-9, the sentence "hESCs are pluripotent and derived from human fertilized eggs, therefore they are free from the risk of immunosuppression and transplant rejection by recipients[16, 31, 32]" contains erroneous expressions. Since hESCs are allogenic to recipients, they cannot be free from the risk of immunosuppression and transplant rejection by recipients. Author should rewrite this sentence as "hESCs are pluripotent and derived from human fertilized eggs, therefore they have a much lower risk of tumorigenesis than iPSCs. Moreover, hESCs reportedly possess immune-privileged properties#1, #2, whose beneficial effects are further strengthened by the advanced intramuscular administration" and so on. #1 Li L et al. Stem Cells 22:448-456, 2004. #2 Drukker M et al., Stem Cells 24: 221-229, 2006

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

ESPS manuscript NO: 25786

Title: Therapeutic potential of human embryonic stem cells in type-2 diabetes mellitus

Reviewer's code: 02446215

Reviewer's country: Italy

Science editor: Xue-Mei Gong

Date sent for review: 2016-03-23 16:41

Date reviewed: 2016-03-30 21:12

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The manuscript represent an original perspective for the use of hESCs. However, due to the innovative concept, the paper needs more detailed description in particular in material and methods section. Have been the cells investigated by molecular approaches in vitro? Have the authors performed differentiation assay? Before the infusion in the patients have been established the cellular phenotype? In addition, in results section, a table illustrating the cellular data will be appreciated.