

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

ESPS manuscript NO: 21665

Title: Use of genetically-engineered pig donors in islet transplantation

Reviewer's code: 00045831

Reviewer's country: India

Science editor: Fang-Fang Ji

Date sent for review: 2015-07-27 11:16

Date reviewed: 2015-08-05 18:49

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> [Y] Accept
<input type="checkbox"/> [Y] Grade B: Very good	<input type="checkbox"/> [Y] Grade B: Minor language polishing	<input type="checkbox"/> [] The same title	<input type="checkbox"/> [] High priority for publication
<input 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 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 type="checkbox"/> [] No	

COMMENTS TO AUTHORS

The manuscript by Bottino et al is well written with a vision to increase available β cell sources and fill the gap for islet transplantation. However to date genetically engineered cells/tissues are not approved in clinical practice. But the concept to employ the latest techniques to generate genetically engineered pigs as islet donors has a long bearing for the human kind. Genetic modifications in pigs may have beneficial effect in reducing IBMIR, rejection under xenotransplant set up. Minor mistake to be corrected (Hyper acute rejection: starting of the paragraph should be One of the major instead of one One the major

Thank you for your comments. In response to your remarks we have made several changes under the category of "Minor language polishing," these include minor changes in grammar as well as a few additional sentences to provide further clarity or better transition between topics, specifically located on page 4 (introduction), at the top of page 7, and on page 10 while discussing IBMIR. Changes have been highlighted in green in the revised manuscript. We have also corrected the error of omission that you indicated ("One of the major" replacing "One the major.") on page 7. This is highlighted in yellow as are the newly inserted references.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

ESPS manuscript NO: 21665

Title: Use of genetically-engineered pig donors in islet transplantation

Reviewer's code: 00070310

Reviewer's country: Japan

Science editor: Fang-Fang Ji

Date sent for review: 2015-07-27 11:16

Date reviewed: 2015-07-28 17:09

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 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 type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

This paper reviewed islet xenotransplantation using pig donors. This is interesting and almost parts are well written. However, it will require some changes before it can be accepted for publication. 1, Please show how to select papers of islet xenotransplantation based on this research. 2, Please show breakthrough or impact as to islet xenotransplantation in this manuscript. 3, This paper requires editorial correction.

Thank you for your suggestions. In regard to question 1, we apologize if we did not fully understand the request. We believe that adding full information, including DOI number to all references when available, will address your comment.

2. We have amended the text on pages 5, 8, and 12, to highlight several breakthroughs in the field (highlighted in yellow). More specifically we deemed of relevance the long-term function of pig islets transplanted to non-human primates and the generation of alpha1,3-Galactosyltransferase knockout pigs. Newly inserted references are also highlighted in yellow.

3. A thorough revision of the language has been carried out, as recommended (highlighted in green)



BAISHIDENG PUBLISHING GROUP INC

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

<http://www.wjgnet.com>

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

ESPS manuscript NO: 21665

Title: Use of genetically-engineered pig donors in islet transplantation

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Reviewer's country: United States

Science editor: Fang-Fang Ji

Date sent for review: 2015-07-27 11:16

Date reviewed: 2015-08-10 12:55

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 type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input 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 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 type="checkbox"/> No	

COMMENTS TO AUTHORS

This paper is generally well written and this Reviewer feels that only minor changes are necessary for this project. The subject - genetically modify porcine donors to enable pancreatic cell transfer into non-humane primate species is highly relevant to the World Journal of Transplantation missions and relevant to ongoing or future human research to occur. The review has an extensive Bibliography and the Authors appear to be recognized experts on the subject. Minor comments about the text: -2nd page, 1st para (in the sentence, which carries Ref #8): change expression "in the clinic" into "in clinical practice" or "clinical medicine" -3rd page, about 1/3 of the page (when describing pig litter sizes) - the Authors state that the phylogenetic difference between human and pig is "approximately 1 million years". That is surely incorrect - even I believe the chimpanzee are separated from human > 2 million years (as no interbreeding can take successfully) - so I suspect pig would be at least an order of magnitude more. Please, check and correct -same comment as the first one for the last paragraph before "Conclusion": change expression of "will not be translatable to the clinic" to "will not be translatable to clinical practice" (or: "will not be translatable to human medical practice/care") In terms of English: minor revision is necessary. In several parts of the paper (1st paragraph of



BAISHIDENG PUBLISHING GROUP INC

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

<http://www.wjgnet.com>

Introduction; 1st paragraph describing of the text after chapter title “Hyperacute rejection: alpha 1,3 galactose (GAL)” or the last paragraph before “Conclusions” are good examples) the sentences are too lengthy and the use of comma are excessive. It would help if an another native speaker of English with a different style would edit the paper further.

Thank you for your comments. We have made some alterations to the language/grammar and in a few instances added additional sentences to act as transition between topics and to provide clarity in order to polish the language sufficiently for publication (highlighted in green). Please see our response to the previous reviewer for more specific details. Additionally, we have made the modifications that you recommend (highlighted in yellow). Specifically, both references to “in the clinic” have been modified to read “in [or to] clinical practice” on page 5 and 12. You are certainly correct in your comment regarding the phylogenetic difference between species and we apologize for not catching this typo. The sentence should have indicated, and now does, a difference of “approximately 100 million years” on page 6. We have also strived to provide further clarity by using smaller sentences without as many linked clauses contained within, particularly in the locations that you indicated would benefit from those changes (Introduction, 1st paragraph after Hyperacute rejection, and the last paragraph before the Conclusion). Newly inserted references are highlighted in yellow.