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## ANSWERING REVIEWERS

**Name of Journal:** World Journal of Transplantation

**ESPS manuscript NO:** 26712

**Title:** Recent insights in the pathogenesis of post-transplantation lymphoproliferative disorders

**Reviewer's code:** 00504150

### Comments to authors

The manuscript entitled, "Recent insights in the pathogenesis of post-transplantation lymphoproliferative disorders by Morscio and Tousseyn is well written, timely and important. I am confused with journal selection. On the title page, it is clearly written as World Journal of Gastroenterology. However, on the invited e-mail for review sent by Lian-Sheng Ma to me, it is stated that this manuscript was submitted to the World Journal of Transplantation. Obviously this manuscript would not fit in the scope of the World Journal of Gastroenterology. It should be for the World Journal of Transplantation. Clarification is needed.

**Reply:** As the reviewer states, the reviewer is meant for the World Journal of Transplantation. "World Journal of Gastroenterology" was erroneously copied from the review template provided online by the journal.

In the abstract, the authors state that they propose stratification of PTLTD according to the histological subtype and the EBV status. The readers would expect detail information regarding a new classification system in the main text. The authors should describe detail about a new classification the authors are proposing in the main text or change the last sentence in the abstract.

**Reply:** In line with the remark of the reviewer, we added more details concerning a new classification to the conclusion of the review.

Minor point: In the abstract the authors use a term "iatrogenic immunosuppression". I would recommend using "chronic immunosuppression" or something like that, because "iatrogenic" implies some sort of mistake or error.

**Reply:** In accordance with the remark of the reviewer, 'iatrogenic' was replaced by 'chronic'.

**Reviewer's code:** 03261799

### **Comments to authors**

The authors review the current literature on the pathogenesis of PTLD, particularly related to the role of EBV. They make a plea for better classification and description of PTLDs. I have the following comments:

#### **Major concerns**

1. This is presented in a manner that makes it very difficult for a transplant clinician to understand. It is perhaps more suited to a haemoncologist, pathologist or a researcher and I fear will not be read by the vast majority of transplant clinicians.
2. The authors assume a considerable degree of prior knowledge from the reader and repeatedly refer them to other reviews to help clarify their position. I think the authors must be more considerate to the reader if they expect anyone to read this paper. The data and its interpretation must be spelled out in a manner that readers can understand with the help of illustrations if necessary. Speaking for myself as a transplant clinician I was no wiser after reading the paper than after reading the abstract and introduction.

**Reply:** We agree with the reviewer that the content of the review can be presented in a more comprehensible way. We adapted the structure of the review and added illustrations to summarize the presented data.

We kept the references to the reviews about management of PTLD and details about EBV protein function and signaling as these topics are not part of the scope of our review and as such we cannot adequately address these issues.

3. The methodology of the review has not been dealt with at all. This is another major flaw. Is the review presenting the authors potentially biased viewpoint or is it a true expression of the available literature on this subject.

**Reply:** In line with the remark of the reviewer we added more details about how the review was written.

#### **Minoir concerns**

1. Some statements regarding the incidence of PTLD and the role of EBV in PTLD are made without references.

**Reply:** A reference to a recent review was added (3. Dharnidharka VR, et al. Post-transplant lymphoproliferative disorders. Nature Reviews Disease Primers. 2016).

2. Unreported data is presented but its source is not provided. Presumably this is from the lab of the author.

**Reply:** As the reviewer states, the unreported data are from our lab.



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**Reviewer's code:** 00503228

### Comments to authors

A major revision is required. The paper is not easy to follow. It should be revised and a consistent approach in the review should be followed.

Some recommendations:

Title: Considering the reviewed literature presented, better to add after colons ": Roles of EBV infection and genetics alterations"

**Reply:** Because the title of this invited review was proposed by the journal board and because the number of words in the title is limited to 12 we could not add the suggestion of the reviewer.

Page 6: "Two early gene expression profiling studies of PTLD produced partly contradictory results..." then what are those contradictory results!?

**Reply:** More details about the results were added to the paragraph.

Page 6: "And how do these disorders relate to lymphoma in the general population?" what disorders? EBV+ vs. EBV-? you can't call them separate disorders now. you may talk about states - paragraphing is very poor. paragraphs need new arrangements.

**Reply:** In line with the remark of the reviewer we changed 'disorders' to 'disease states'.

The literature review under any subcategory is not consistent and sometime confusing. Subcategories and discussions need to be reorganized. For example "Craig et al. suggested ...." under subcategory of "EBV- PT-DLBCL is biologically similar to DLBCL in the general population" is nonsense. There are several instances of these.

Subcategories should be named in full words not abbs. - page 9 "also the results ..." bring all the data associated with genetic alterations under its respective subcategory, , and here you can have a brief reference to them.

**Reply:** In line with the comments of the reviewer the structure of the review was changed.



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**Reviewer's code:** 00054465

### **Comments to authors**

A very well thought out review