Author's response to reviews

Title: HIV-1 Tat Protein Alter the Tight Junction Integrity and Function of Retinal Pigment Epithelium: an in vitro Study

Authors:

Ling Bai (larkling@163.com)
Zhenping Zhang (zhenpin.z@hotmail.com)
Hui Zhang (hui.zhang@jefferson.edu)
Xiumei Li (Xium.lee@gmail.com)
Qiurong Yu (QiuR.yu@gmail.com)
Haotian Lin (haot.lin@hotmail.com)
Wenhui Yang (wenhui.yg@gmail.com)

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Author's response to reviews: see over
Dear Dr. Rikki Graham

Thank you for your message concerning our manuscript entitled "HIV-1 Tat Protein Alter the Tight Junction Integrity and Function of Retinal Pigment Epithelium: an in vitro Study" (BMC Infectious Diseases Ms. No.: 1375774087181044). We also appreciate the reviewers’ kind comments on our manuscript and valuable suggestions to improve it. We fully dealt with the criticisms in the revised manuscript and underlined all the changes.

**Referee 1: 2093810998198664_comment**

*Minor comments*

1) Page 14 lane 1 should be modified as: ...Tat was able to induce…

**Answer:** Thank you for your helpful suggestion. We have revised it.

2) Page 15, last paragraph of results describes Figure 9 and not 8.

**Answer:** There are too many figures in this manuscript, so it maybe little confusing for the reviewer. The last paragraph of results described the effects of PDTC and PD98059 inhibit NF-xB DNA binding activity, which showed in Figure8. Figure 9 is to show the effects of PDTC and PD98059 on HIV-1 Tat induce destruction of barrier.

3) In the Discussion the Authors cannot state that: “We future determined whether these pathways are involved in the regulation of claudins expression that was observed in the present study”, since this study does not provide any link between ERKs and/or NFkB activation and claudins expression. It is more correct what is stated in the abstract that:” The effects of HIV-1 Tat on barrier function of the RPE may be mediated by ERK MAPK and NF-#B activation…”, unless the Authors will determine expression levels of claudins upon treatment with Tat in the absence or presence of ERKs and NFkB inhibitors.

**Answer:** We really appreciate the rigorous attitude of reviewer. We have addressed in the original manuscript about the expression levels of claudins upon treatment with Tat in the presence of ERKs and NFkB inhibitors, which in page 14, last paragraph, and Figure 4, 5.
Referee 3: 1777667683199669_comment

The revised manuscript is satisfactory. However, the manuscript still have grammatical / English errors.

Abstract
Line 1 “How HIV-1 entry into the eyes remain obscure” should be “How HIV-1 enter into the eyes remain obscure”
Line 3 “..by which contributes to HIV trafficking into the eyes.” Should be “..and contributes to HIV trafficking into the eyes”
Line 8 “After treated with HIV-1 Tat protein,” should be “After treating with HIV-1 Tat protein,”

Background
Page 5. Line 2: “ RPE is also one of the cells targeted by HIV target,” should be “RPE is also one of the cells targeted by HIV,”

Methods
Reagents: “phosphor-ERK” should be “phospho-ERK”

Results
Page 13.
Line 8 “occluding” should be “occludin”
Line 17: “HIV-1 Tat Induces Promotes ERK phosphorylation and NF-#B DNA binding activity in RPE” should be “HIV-1 Tat Induces ERK phosphorylation and Promotes NF-#B DNA binding activity in RPE”

Discussion.
Page 15, last line: “by which contributes to HIV trafficking into the eyes.” Should be “ and contributes to HIV trafficking into the eyes.”

Page 17
Line 5. “The relationship TJs and the oBRB during HIV infection still need to be elucidated.” Should be: “The relationship between TJs and the oBRB during HIV infection still need to be elucidated.”
Line 14. “We future determined….” Should be: “We further determined…”

Page 18, line 15: “NF-#B is not thought to be transcription factor activated by ERK MAPK” should be “NF-#B is not thought to be a transcription factor activated by ERK MAPK”.

Answer: Thank you very much for your careful review. I have revised mistake you mentioned.

We appreciate all the comments and suggestions from the reviewers. We are glad to know that you accept the manuscript for publication in BMC Infectious Diseases.

Sincerely,

Zhenping Zhang