



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>

Name of Journal: *World Journal of Clinical Infectious Diseases*

ESPS Manuscript NO: 20376

Manuscript Type: Review

Response to Reviewers Letter

Reviewer One

1. In the Introduction, first paragraph, the sentence "Each protein is multifunctional and sufficient to enable efficient replication of virus in susceptible cells." Seems confusing to me, as it "sounds" that even if a virus has only one of either of these proteins – that is sufficient for it replicate. If indeed this is the case (which I assume it is not), please add a relevant reference.

Response: We apologise for this and the section has been clarified to state that the expression of all 5 viral proteins is sufficient to enable efficient replication of virus: "Each protein is multifunctional and expression of these five proteins is sufficient to enable efficient replication of virus in susceptible cells."

2. Define ASC when first mentioned.

Response: This is defined page 8, line 17.

3. Page 7, "[46]" should be superscript.

Response: changes to superscript.

4. Page 10, first paragraph: revise "a potential".

Response: revised.

5. Reference 78: correct to "in India".

Response: Corrected.

6. Maybe add another figure that describes a) the suggested areas that need further studies to elucidate the interplay between the RABV and the immune system and b) the potential suggested interventions that may enhance successful clearance/therapy of RABV infection.

Response: We have modified figure 2 in line with reviewer 2 comment and added potential points where further studies are required.

Reviewer Two

The review concludes:

1. Neutralising antibodies are the main correlates of protection against rabies virus infection. - **agree**
2. For the induction of neutralizing antibodies, strategies to enhance RABV replication in the periphery are important. **Partially agree, enhanced stimulation of the immune system (periphery or CNS) is needed. How this is achieved (vaccination?) is still unclear in the context of rabies virus infection.**
3. Then, the strategies to transfer the neutralizing antibodies to the CNS are critical for the effective immune responses. **Agree, but this follows 2, if there is no immune response to transfer into the CNS there is a problem.**

More detail description of the current trials or the rationale of these strategies will help readers to figure out the issues in protection against rabies virus infection.

Response: Unfortunately, such trials have not been published so they cannot be reviewed in this paper. Recent attempts that are in the public domain are included in the Conclusion section.

Minor points:

1. Page 2, line 4. "the Central Nervous System (CSN) reads "the central nervous system (CNS)".

Response: corrected.

2. Page 4, line 6 from bottom. Spell out "VNSs" correctly when it appears at the first time.

Response: corrected.

3. Page 7, line 7, [46] should be superscript.

Response: corrected

4. Page 8, line 11, spell out "CSF".

Response: Spelt out.

5. Page 8, line 15, "neurotropic" reads "neurotropic".

Response: Corrected.

6. Page 8, line 17, spell out ASC - antibody secreting cells?

Response: Spelt out.

7. Page 10, line 7, add "of" after "The role".

Response: Inserted.

8. Page 10, line 12. "cerebrospinal fluid (CSF)" should be "CSF" here. Spell it out at page 8, line 11.

Response: Corrected.

9. Page 10, line 15, 16, authors stated that "CSF antibody is detected relatively late stage in the course of infection (Table 1)." But table 1 that CSF antibody was found only in one case. Reconsider the description. Table 1 (p20).

Response: the column heading has been revised to "Findings of tests to detect neutralizing antibody in CSF".

10. "Tables 1" in the title reads "Table 1".

Response: Corrected.

11. What is "EBLV2"?

Response: EBLV-2 is European bat lyssavirus 2, a lyssavirus detected in UK bats. A footnote to this effect has been added to the table.

12. Figure is too simple.

Response: We disagree with this comment. Further detail would over-complicate the figure. However, we have modified the figure to added points where further investigation is required as suggested by reviewer 1.

13. Add more information about loci of mutations of live-attenuated viruses.

Response: This information has been added to the legend of figure 1.