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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Virology
ESPS manuscript NO: 10716
Title: Nuclear Factor kappaB? (NF-kB) Represses the Expression of Latent Membrane Protein 1 in Epstein-Barr Virus Transformed Cells
Reviewer code: 02615858
Science editor: Fang-Fang Ji
Date sent for review: 2014-04-16 13:31
Date reviewed: 2014-04-25 18:11

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Rejection
[ ] Grade E: Poor		[ ] Existing	[ ] Minor revision
		[ ] No records	[Y] Major revision

COMMENTS TO AUTHORS

In this report, Cao et al have analyzed the expression of the Epstein-Barr virus (EBV) latent membrane protein-1 (LMP1) through NF-kappaB proteins in EBV-transformed cells. The research is well conceived and correctly carried out. Based on their results, the authors claim that NF-kappaB acts as a negative regulator of LMP1 expression, rather than behaving as an activator (as reported by others). Their data seem to be, however, rather preliminary and do not allow such straightforward general conclusion. Moreover, the NF-kappaB inhibition of LMP1 expression is not unequivocally demonstrated in EBV-transformed cell background. Specific comments: 1. It is well-known that NF-kappaB activity is fine-tuned by positive and negative regulators as well as by post-translational modifications. At least, levels of NF-kappaB proteins and their subcelullar location should be determined in IB4 cells and shown in Figs 1 and 2. Another protein (or other proteins) classically known to be regulated by NF-kappaB should be examined as control(s). 2. It is not clear why "the minimum time" for the induction of IkappaB was determined and how "this" was tested. The authors should clarify these points in the manuscript. 3. LMP1 expression decreases from 6 h in IB4 cells either grown with or without tetracycline (Fig. 1). An explanation to this issue should be given. What are the levels of LMP1 and IkappaB at time 0? The amount of IkappaB at different times should be shown, particularly because of the 24-h delay in NF-kappaB inhibition required for the induction of IkappaB as it has been reported elsewhere (Cahir-McFarland et al, Pro Natl Acad Sci USA, 2000,

97:6055-6060; Cahir-McFarland et al, J Virol, 2004, 78:4108-4119). 4. In Fig. 2, as was pointed out above, overexpression of NF-kappaB should be confirmed in IB4 cells. Whether the experiment was performed with or without tetracycline should be indicated. How long did it take the isolation of CD4-positive cells? Was it performed in the presence or absence of tetracycline? Under the conditions used, what is the actual amount of IkappaB? What effect would be expected if the expression of IkappaB were to be induced? 5. Relative LMP1 and IkB levels should be quantify and shown in Figs 1 and 2. 6. To make the results of LMP1 promoter activity in 293T cells upon overexpression of LMP1, LMP-DM and NF-kappaB (Figs. 3 and 4) more comparable to those described by others, shorter promoter regions (or even larger) should be analyzed. Additionally, overexpression of LMP1, LMP-DM and NF-kappaB proteins should be confirmed and shown. 7. Statistical analyses should be performed and described in the Materials and Methods section. Statistical significance should be indicated in Figs 3 and 4. 8. The authors should also discuss their results considering those obtained by Cahir-McFarland et al (Pro Natl Acad Sci USA, 2000, 97:6055-6060), in which LMP1 expression was not affected by inhibition of NF-kappaB (using the same cell line). 9. Data obtained by using the NF-kappaB inhibitor BAY11-7082 are not reported in the Results section; therefore they should not be mentioned in the Discussion section as "Data not shown". Should they either be incorporated in the corresponding section or refer to them as "Zhang L, personal communication" or "unpublished results", or give an appropriate quotation. Minor points: 1. Materials and Methods Section. The descriptions of the CD-4 and b-galactosidase expression plasmids are missing. 2. p 4, 3rd paragraph, line 3. Please indicate a brief description for NF-kappaB reporter construct or a reference. 3. p 5, 1st paragraph, first line. Quote the reference of tubulin antibody. 4. p 5, last line, p 6, first line "…while CD4-positive cells are attached to the wall of…" It should be indicated as "attached to Dynabeads CD4" instead. 6. p 6, 2nd paragraph. Used dilutions of primary antibodies should be given. References and dilutions of secondary antibodies shoul

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COMMENTS TO AUTHORS

My comments to World Journal of Virology In this paper, authors found that NF-κB likely negatively regulated LMP1 expression in EBV-transformed cells, and LMP1 might negatively regulate its own expression through NF-κB, which suggested as a classical feedback inhibition. The study design and paper writing are OK. The methods provided in this study are corrected. However, there are some flaws needed to be revised. Major 1.As the study suggested, NF-κB negatively regulated LMP1 expression in IB4 cells, but some reports got different conclusions, the reasons could be drawn as genetic differences in cell lines, type of assays, et al. Then what're the expression levels of LMP1 in other EBV-transformed cell lines with the same conditions? You'd better have a try. Minor 1.Some spelling errors could be found in the paper. 2.How to determine the minimum time for the induction of IκB? What's the standard? Decision: Minor Revision