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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 Virology
ESPS manuscript NO: 22470
Title: ICP0 functional domains and their coordination in herpes simplex virus replication
Reviewer's code: 02446947
Reviewer's country: Australia
Science editor: Jin-Xin Kong
Date sent for review: 2015-09-07 08:38
Date reviewed: 2015-09-20 12:34

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

COMMENTS TO AUTHORS

Overall the review by Haidong Gu on the multiple functions of HSV-1 ICP0 is a nice summary of the field and does well in incorporating the diverse and complex roles of ICP0. Major corrections: 1) ICP0 has been detected in the tegument of virions, and may be recruited (along with ICP4) initially to intranuclear capsids (via the E3 ubiquitin ligase domain) as well as in the cytoplasm to capsids during HSV-1 assembly, and is therefore part of incoming viral proteins delivered during entry (studies by the labs of Lippe and Nicola). This should be mentioned along with the possible role (eg targeting capsids to the nucleus during entry, Delboy and Nicloa 2011 J Virol) of incoming ICP0 prior to de novo synthesis. 2) A comment on ICP0 homologues found in other Herpesviridae members would be helpful 3) Need to incorporate recent publications on ICP0 listed below into the review Pozhidaeva AK, Mohni KN, Dhe-Paganon S, Arrowsmith CH, Weller SK, Korzhnev DM, Bezsonova I. Structural Characterization of Interaction between Human Ubiquitin Specific Protease 7 and Immediate Early Protein ICP0 of Herpes Simplex Virus-1. J Biol Chem. 2015 Jul 29. pii: jbc.M115.664805. [Epub ahead of print] Smith S, Weller SK. HSV-I and the cellular DNA damage

response. Future Virol. 2015 Apr;10(4):383-397. Sloan E, Tatham MH, Groslambert M, Glass M, Orr A, Hay RT, Everett RD. Analysis of the SUMO2 Proteome during HSV-1 Infection. PLoS Pathog. 2015 Jul 22;11(7):e1005059. Taylor KE, Mossman KL. Cellular Protein WDR11 Interacts with Specific Herpes Simplex Virus Proteins at the trans-Golgi Network To Promote Virus Replication. J Virol. 2015 Oct 1;89(19):9841-52. 4) For the ICP0 interactions listed were they confirmed by more than one assay and if so this should be highlighted in the text. 5) In figure 1 need to illustrate that there are actually 2 copies of the ICP0 gene in the HSV genome 6) It would be very desirable to have an additional figure summarizing the interaction partners of ICP0, where they bind ICPO, and the function of the interaction in the context of viral replication. Minor corrections (relevant section names in italics): 1) Abstract "gene product" to "gene products" "the HSV-1 pathogenicity" to "HSV-1 pathogenicity" 2) Introduction "opportunistic pathogen" to "opportunistic pathogens" clarify the term "unusual shift of ICP0" "a yeast-2-hybrid screenings" to "yeast 2-hybrid screenings" "to coordination" to "coordination" 3) ICP0 gene structure when referring to "ICP0 gene" in this section change to "the ICPO gene" "to latency-associated" to "the latency-associated" 4) 1. RING finger domain and E3 ubiquitin ligase activity Clarify the statement: "The structure of ICP0 RING finger has been demonstrated by nuclear magnetic resonance (NMR) (34), but the crystal structure has not yet been solved." Is there an issue with the NMR structure that there is an absolute need for a crystal structure? "for at least 1000 folds" to "at least 1000 fold" "over viral outcome" to "overall viral outcome" 5) 2. Nuclear localization domain and ICP0 nuclear/cytoplasmic translocation "presence of NLS. Once inside nucleus" to "presence of the NLS. Once inside the nucleus" "see section for" to "see section on" Clarify if there is an NES motif in ICP0? 6) 3. Proline-rich region and ND10-fusion "proline-rich region" to "proline-rich regions" "ND10-fucion" to "ND10-fusion" "with SH3" to "with an SH3" "indicate the importance of ND10-fusion" to "indicates the importance of the ND10-fusion" 7) 4. SUMO interaction motif and ICP0 substrate recognition "SUMO moiety" to "The SUMO moiety" "SUMO-interaction" to "the SUMO-interaction" "contain SIM" to "contain a SIM" "scattering throughout ICPO" to "scattered throughout the ICP0" "ICP0 ability" to "the ability of ICP0" "PML (108) suggesting" to "PML (108). This suggests" 8) 5. ICP0 C-terminus and a diverse array of functions "The C-terminus of ICP0, br

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ESPS PEER-REVIEW REPORT

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[Y] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[Y] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
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[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Though all the information in the paper is important and highly relevant, the reviewer feels that the author did no clarify enough the historic stepwise evolution of related research (as already mentioned above). The reviewer would recommend to add a Table listing the important facts in a simple overview The reviewer would recomment to add a Table listing the important facts in a simple overview The reviewer would recomment to add a Table listing the important facts in a simple overview Domain Localization (aa.) Activity Function I believe the author will understand how to prepare such a Table. The Conclusions are fine and well written. The reviewer` s remark: the specific features of latency established in semipermissive neurons are not mentioned. The HSV DNA in them may go dormant from the very beginning in the absence of any virus replication. What is the precise role of ICP0, in contrast to ICP4, in neuronal latency? According to reviewer`s experienece, ICP4 mRNA but not ICP0 mRNA could be found in non-cultured ganglia, i.e. prior to reactivation. ICP0 gene transcription is an indicator of the onset of reactivation (see Rezuchová I et al., in Intervirology 2003, 46: 25-34).

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ESPS PEER-REVIEW REPORT

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
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		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

In this review, the author summarized the knowledge of ICP0 according to the four aspects: the timeline of revealing ICP0 activities; ICP0 gene structure; ICP0 protein: domains and functions; post-translational processing of ICP0. I think the author did collect and read a huge number of recent references and also try to present a significant review in this filed. However, it is better to avoid a literature review to be an annotated bibliography in which you summarize briefly each article, and the readers could not find the key point and focus of the article. Since ICP0 is a multifunctional protein, it is hard to include all aspects in one manuscript. I would suggest the author could consider reorganizing the manuscript, narrowing the scope and selecting one or two aspects as a focus to expound. Meanwhile, ICP0 has an important role in latent infection establishment and recurrent infection. But in this review, the author only described the role of ICP0 in the acute phase of infection, and did not mention the function in the latency. In addition, charts and diagrams are recommended to use to help readers understand more clearly.

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ESPS PEER-REVIEW REPORT

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
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COMMENTS TO AUTHORS

ICP0 is a unique multifunctional protein which plays a crucial role in HSV-1 infection. This manuscript makes an extensive review on functional domains of ICP0 through describing individual domains, their biochemical properties and their coordination in virus-host cell interaction. Additionally, ICP0 is under regulation at transcriptional, post-transcriptional and post-translational levels. Information on the transcriptional, post-transcriptional regulation of ICP0 could be added to the manuscript to make a more complete delineation. Overall this is an interesting review and should be accepted for publication in this journal.