

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Experimental Medicine

ESPS manuscript NO: 14408

Title: Cytomegalovirus (CMV) and human brain tumors; role in pathogenesis and potential treatment options

Reviewer code: 00504885

Science editor: Xue-Mei Gong

Date sent for review: 2014-10-05 12:14

Date reviewed: 2014-10-11 01:50

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This review argues that HCMV could be related to tumorigenesis. It is generally an interesting review and provides significant information for readers. I highly recommend it to the journal for publication. Some minor points are listed as below. 1. The word "Evidence" has been used very often, sometimes as singular, sometimes as plural, please make it even in the text. 2. The title contains a ";", it should be ":". 3. The authors state: "However, stimulation of dendritic cells with glioblastoma tumor lysates leads to expansion of CMV specific T cells in glioblastoma patients, and CMV pp65 specific T cells can kill autologous glioblastoma cells in vitro, which provide indisputable immunological evidence that CMV epitopes are present in glioblastoma tumors." This statement is uneasy to understand, the authors need to describe the logics in detail. 4. Ref.#99 and #109 are the same. Please check if there are any other repetitive references.

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Name of journal: World Journal of Experimental Medicine

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Title: Cytomegalovirus (CMV) and human brain tumors; role in pathogenesis and potetial treatment options

Reviewer code: 00504253

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This review summarized that CMV may play a pathogenic role in cancers of epithelial and neuronal origin. Under such circumstances, anti-viral treatment strategies may provide new options in cancer therapy of CMV positive tumors and metastases to improve patient outcome. The manuscript was well written with enormous supporting data. However the role of CMV in human brain tumors is so controversial that authors need to pay more attention to the opposite view point. Authors need to add reasons why many researchers failed to detect CMV in tumor in more details. This manuscript is acceptable with minor revision.

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Experimental Medicine

ESPS manuscript NO: 14408

Title: Cytomegalovirus (CMV) and human brain tumors; role in pathogenesis and potetial treatment options

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

In their review article, S?derberg-Nauclér and Johnsen summarize basic informations as well as recent findings on the potential role of human cytomegalovirus (CMV) infection in human brain tumor (glioblastoma and medulloblastoma) pathogenesis. This is a timely and well-written article that deserves publication, although I strongly suggest considering the following points: 1. The manuscript is strongly biased in favor of an active role of CMV in brain tumor oncogenesis or oncomodulation. However, such a role is far from being established. I urge the authors to assess the potential contribution of CMV to brain tumor pathogenesis in a more balanced fashion. Otherwise, this article will be an opinion piece rather than an actual review. For example, the authors state that "over 90% of these tumors are positive for CMV proteins and nucleic acid" (page 3) and that there is "indisputable evidence ... that CMV is present in brain tumors" (page 13). However, the actual numbers present in the literature range from 0 to 100% of CMV-positive brain tumors. Saying that "The development of this field is though hampered by the fact that some researchers have failed to detect CMV in tumors" (page 3) sounds a bit as if a minority of ignorants is blocking progress in this area, because they are too stupid to detect CMV (casually speaking). This is not the case, since numerous laboratories tried hard but failed to detect CMV DNA in brain tumor tissues despite using highly sensitive PCR techniques. Likewise, as the authors know, the early work on the transforming and oncogenic activity of CMV (page 8-9) is highly controversial. Finally, CMV not only has



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positively oncomodulatory potential, but may also affect tumor cell biology including proliferation in negative ways. For instance, CMV has long been known to block cell cycle progression (e.g., Wiebusch & Hagemeier, 1999, J. Virol. 73) and the virus may not just induce (page 10) but also disrupt IL-6 signaling (Reitsma et al., 2013, J. Virol. 87). 2. Along the lines of point 1., it should not be ignored that the study published in reference 116 has been met with criticism (Hellstrand et al., 2013, N. Engl. J. Med. 369; Wick et al., 2014, Int. J. Cancer 134). 3. Although largely well written, the text contains a number of small grammatical and other errors that should be removed by proof-reading the entire manuscript. Examples include, but are not limited to: “recent evidence also imply that ...” (Abstract), “... antiviral therapies against CMV needS to be revisited ...” (Abstract), “which imply that this virus” (page 3), “emerging evidence also imply ...” (page 3), “... imply the unlikelyhood that this virus represenT ...” (page 3), “... IT seems to be a strong inverse relationship ...” (page 7), “... that activateS transcriptional programs ...” (page 7), “... and provideS immune evasion strategies” (page 9). 4. One or more diagrams illustrating key aspects discussed in this manuscript would make reading more enjoyable.