

November 11, 2014

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 14408-review.docx).

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

**Authors:** Cecilia Söderberg-Nauclér and John Inge Johnsen

**Name of Journal:** *World Journal of Experimental Medicine*

**ESPS Manuscript NO:** 14408

The manuscript has been improved according to the reviewer's suggestions.

1 The format has been updated

2 A revision has been made according to the suggestions of the reviewer's:

Reviewer # 00504253: In the revised manuscript we have discussed the potential reasons for the discrepancies between different research groups results regarding the detection of CMV in tumor samples. This discussion has been added on page 4 in the revised manuscript.

Reviewer # 00504885:

- 1) In the revised manuscript the word "evidence" has been changed to suggest or indicate and when used the correct grammatical form is used.
- 2) The title has been corrected to "Cytomegalovirus (CMV) in human brain tumors: role in pathogenesis and potential treatment options."
- 3) The sentence reading "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." Has been changed to "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. This suggest that CMV epitopes are present in glioblastoma tumors"
- 4) Reference 99 and 109 has been corrected. The reference list has been checked for errors in the revised version and should in its present form be correct.

Reviewer # 00504107:

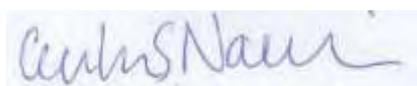
- 1) In the revised manuscript we have added discussions regarding the failure to detect CMV in tumor samples and discussed the potential reasons for this (see comments to reviewer # 00504253 and changed made on page 3 in the revised manuscript). The words "indisputable evidence" and "evidence" have been substituted with the words "suggest" or "indicate" in the revised manuscript.

- 2) We are fully aware about the criticism regarding reference 116 (reference 115 in the revised manuscript) and have commented that new trials including larger glioblastoma patient populations should be performed with anti-CMV drugs as an add-on therapy.
- 3) The revised manuscript has been thoroughly checked for misspellings and type errors.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Experimental Medicine*.

Yours Sincerely,

A handwritten signature in blue ink, reading "Cecilia S. Nauclér". The signature is written in a cursive style and is placed on a light blue rectangular background.

Cecilia Söderberg-Nauclér , MD, PhD

Professor

Department of Medicine, Solna,

Center for Molecular Medicine,

Karolinska Institutet, 171 76,

Stockholm, Sweden

E-mail:Cecilia.Naucler@ki.se