Reviewer's report

Title: Profound tumor-specific Th2 bias in patients with malignant glioma

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Reviewer: Kathrin Bauer

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Revision „Profound tumor-specific Th2 bias in patients with malignant glioma“, Shimato et al. BMC Cancer

The manuscript by Shimato et al. describes the detection and characterization of CD4-positive T cell responses against glioma-associated antigens in the peripheral blood of GBM patients, meningioma patients and healthy donors. This work represents a comparative study regarding the release of IFN-gamma and Interleukin-5, as markers for a Th1 and Th2 response, respectively, upon stimulation with 5 glioma-associated peptides derived from MAGE and IL-13. The authors observed that antigen-specific T cells could be induced in PBMCs from healthy donors, meningioma patients, primary GBM patients, recurrent GBM patients and that in contrast to healthy subjects and meningioma patients, peripheral T cells from GBM patients displayed a pronounced Th2 bias.

General comments:

The manuscript is clearly written and the methods used are appropriate and well described. However, some points should be considered:

Major Compulsory Revisions

1) Why did the authors use PBMCs for stimulation and did not further isolate T cells, B cells and monocytes? This should be discussed. A stimulation of 14 days is too short to talk about T cell lines, particularly without phenotypic characterization of the cells, for example by FACS analysis.

2) The manuscript would clearly benefit from an additional ex vivo analysis of day 0 T cells to exhibit that the analyzed epitopes are relevant in the GBM setting and to reveal that the same bias towards Th2 responses can be detected regarding memory T cells.

Minor Essential Revisions

3) In the section “Responses to HLA Class II-restricted peptide stimulation” on page 10, the significant p-value is given as 0.5. This should be corrected.

4) One aim of the study was to detect the CD4-positive T cells against the analyzed antigens in the peripheral blood of glioma patients. This should be included in the results part of the abstract.
5) It would be helpful to mention the selection criteria for the analyzed peptides already in the Methods section (page 6).

6) Throughout the manuscript the authors are talking of glioma patients, however, only GBM patients have been included in the study. This should be clearly stated in the figures.

7) The authors should explain why they added amino acid substitutions in the analyzed peptides and discuss the limitations that follow from these modifications.

8) The authors should explain why they used the geometric mean not only for comparison of IFN-gamma/IL-5 ratios but also for comparison of cytokine levels.

9) The differences between healthy subjects and glioma patients regarding the cut-off definition (page 10) should be explained. What was the cut-off for meningioma patients?

10) Meningioma patients should also be listed in table 2.

11) The discussion and conclusion of the data are a little bit unbalanced and the conclusion that “glioma patients are unlikely to have the capacity of favourably respond to immunization against tumor antigens ….” is too general and is, stated like this, not supported by the data. These paragraphs should be adapted.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.