Reviewer's report

Title: Therapeutic Limitations in Tumor-specific CD8+ Memory T Cell Engraftment

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Reviewer: William Gillanders

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Accept without revision

Comments to Authors

This manuscript is clearly written and the conclusions are very straightforward. Strengths of the manuscript include a well-defined adoptive transfer model system, well-designed experiments with appropriate controls, results that are clearly presented, and a balanced discussion. Weaknesses of the manuscript include lack of innovation, and conclusions that will have a limited impact. This manuscript will be of interest primarily to investigators in the field of tumor immunotherapy. Overall, I believe that this manuscript is suitable for publication in BioMed Central Cancer.

Is the question posed by the authors new and well defined?
Defining the mechanisms of immunotherapy failure remains an area of active research interest. The authors have used a T cell receptor transgenic adoptive transfer approach. Unfortunately, the results are not novel - low effector cell concentration and antigen loss appear to be the dominant mechanisms of tumor escape. The experiments addressing precursor frequency are particularly weak. The experimental design largely assures that at some point the precursor frequency will be too low to be of therapeutic benefit. Therefore the conclusion that sufficient numbers of cells are required is largely trivial. It might have been informative to determine what happens to these cells in vivo. Do they proliferate? Are they present at the tumor site? The experiments addressing antigen loss are more thorough and informative. Defining the characteristics of the individual E.G7 clones is particularly valuable. Overall the data clearly support the authors' hypothesis that tumor escape is a result of overgrowth of an antigen-loss variant of E.G7.

Are the methods appropriate and well described, and are sufficient details provided to replicate the work?
The experimental design is straightforward and well described. This work could be readily replicated.

Are the data sound and well-controlled?
Overall, the data are sound and the controls are appropriate. The results of figure 3 might be more informative if they were normalized to account for the number of OT-1 T cells in each condition.

Does the manuscript adhere to the relevant standards for reporting and data deposition?
Yes, although the applicability of data deposition to this manuscript is limited.
Are the discussion and conclusions well balanced and adequately supported by the data? The discussion is balanced, and the authors do a nice job of reviewing the relevant literature. They acknowledge the limited impact of the article.

Do the title and abstract accurately convey what has been found? Yes.

Is the writing acceptable? Yes. Only a few minor typographical errors are noted.

**Competing interests:**

None declared.