Reviewer's report

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

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Reviewer: Andreas Mackensen

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

Advice on publication: Reject

The paper written by Bathe and colleagues deals with the adoptive immunotherapy of tumor-specific CD8+ memory T cells in a mouse tumor model. Although this study addresses some interesting questions it does not really contribute critical new mechanism-driven information. It has been previously shown that different numbers of CD8+ T cells play an important role for tumor rejection (Cordaro et al. 2000; Dent et al. 1989). The further notion of tumor escape of low antigen expressing tumor clones has also been described previously (Bodmer et al. 1989; Spiotto et al. 2002). Furthermore I disagree to assume a tumor-free mouse model with adoptively transferred T cells resembling the clinical situation of a patient with minimal residual disease after tumor burden resection.

Further comments:
Fig 1: The experimental design is according to standards. Nevertheless it seems that in the group of 2M CTL transferred some animals are missing (curve ends at 0.35%)
Fig 3: The experiment does not exclude a major fraction of the transferred T cells being anergic, as a 20-fold number of transferred T cells leads only to 3-4 fold cpm. Perhaps a combination of cell numbers and percentage of IL-2 producing cells upon stimulation might be helpful.
Fig 4+5: Data are convincing, but indicate a insufficient cloning after the transfection, as the authors mention. The data support the general accepted notion that tumor outgrow from antigen-loss variants is more likely (Tanaka et al 1988, Wortzel et al 1984).

Competing interests:
None declared.