Reviewer's report

Title: Systemic treatment with CAR-engineered T cells against PSCA delays subcutaneous tumor growth and prolongs survival of mice

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Reviewer: Richard Koya

Reviewer's report:

The authors developed a third generation CAR against the prostate stem cell antigen (PSCA) in a lentiviral vector platform. They showed that T cells transduced with the vector specifically recognized PSCA-overexpressing Mel526 melanoma cells by different in vitro assays. Adoptive T Cell transfer of PSCA CAR-T cells delayed tumor growth in an NMRI nude mouse model. The relevance of the approach in potentially helping prostate cancer patients is hampered by the lack of evidence in prostate cancer tumor/cell lines, since the authors showed that surface PSCA expression is undetectable in a panel of prostate ca. cell lines.

Major Compulsory Revisions

1) Fig 1B: T cells transduced with lentiviral (empty) vector backbone would be a better control than just comparing to untransduced cells. Please show the data.

2) Fig 2: Results comparing lentivector control-transduced (or at least with untransduced T cells) against PSCA CAR- T cells must be shown.

3) The major weakness of the article is the lack of evidence in the intended target cancer cells (prostate ca. tumors). Surface PSCA expression in various prostate cancer cell lines was undetectable in vitro, but how about its expression in xenografts in mice? (Do they still lack expression of the antigen or do they "regain" expression in vivo as described in the literature?). The authors should show some studies/data on this approach and perform adoptive T cell transfer in these mice.

4) Fig.4: Please show data using control mel526 or mel526 (TARP) xenografts to allow better comparative studies.

Minor Essential Revisions

1) The authors should submit the DNA or Aminoacid sequence of the CAR for proper evaluation as supplemental data.

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.