

Dear Editor,

We have studied the valuable comments from you, the assistant editor and reviewers carefully, and tried our best to revise the manuscript. The point to point responds to the reviewer's comments are listed as following:

Major comments:

1. The authors suggest that LAP+CD4<sup>+</sup> T-cells have a superior immunosuppressive ability than CD4<sup>+</sup>CD25<sup>+</sup>T-cells. However, the authors chose to look solely on the characteristics of this cell population, ignoring the immune activation status of the tumor and its microenvironment. It would be essential to know the proportion of tumor-infiltrating and peripheral CD8<sup>+</sup> T cells, as well as the expression of immune effector molecules, such as Granzyme B and Perforin.

**Response:** Thank you for your valuable and thoughtful comments. The next step in our research is to focus on the relationship between CD8<sup>+</sup> cytotoxic T lymphocyte (CTL) and LAP+CD4<sup>+</sup> T-cells, as well as the expression level of immune effector molecules, such as Granzyme B and Perforin, in tumor immune microenvironment.

2. The cohort size is relatively small, which is why the confidence interval for the statistically calculated clinical values should be shown (Table 3).

**Response:** Thank you for your valuable advice, we have filled the 95% CI in the Table 3.

Minor comments

1. Figure 1: isotype control samples should be shown for each of the flow cytometry plots due to the different sizes of the gates.

**Response:** Thank you for your careful reading of our manuscript. we have added the flow cytometry plots of isotype control samples in Figure 1A .

2. Due to English not being the first language of the authors, there are several typos, and some sentences that are unclear:

- This is the first time that isolated LAP+CD4<sup>+</sup> T cells by using this method
- The inhibit immune function of LAP+CD4<sup>+</sup>T cells are more potently than traditional CD4<sup>+</sup>CD25<sup>+</sup>Foxp3<sup>+</sup> Treg cells

**Response:** Thank you very much to point out the sentence structure and grammatical issues in our manuscript. According to the comments, we polished the manuscript with a professional assistance in writing, conscientiously.

3. The importance of CEA as a marker was not explained

**Response:** Thank you for your valuable advice, We have explained the importance of CEA in the new manuscript.