1067P - Discovery of a new CD4⁺ T cell cluster that correlates PD-1 blockade efficacy
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Backgrounds
CD4⁺ T-cell immunity, which helps clonal proliferation, migration, and cell-killing activity of CD8⁺ T cells, is essential in antitumor immune responses. To identify the CD4⁺ T cell clusters responsible for antitumor immunity, we simultaneously analyzed the naïve-effector state, Th polarization, and T-cell receptor (TCR) clonotype based on single-cell RNA sequencing data.

Results

Figures

- **Fig. 1.** Clustering of CD4⁺ T cells according to ISNE1, ISNE2, and ISN3. A. Unsupervised clustering analysis of the T cell population. B. Clustering of naïve-effector T cells based on CD39/CD62L. C. Clustering analysis of TCR clonotype on CD4⁺ T cells.

- **Fig. 2.** Cell identification of CD4⁺ T cell clusters based on the expression of CD28 and CD122. A. CD4⁺ T cell populations are shown. B. CD28 and CD122 expression of TCR clonotypes.

- **Fig. 3.** T lymphocyte mapping according to CD80 expression and CD196 expression. A. T cell lymphocyte mapping based on CD196 expression and CD80 expression. B. T cell lymphocyte mapping based on CD196 expression and CD4⁺ T cell clonotype.

- **Fig. 4.** Th cell cluster based on expression of CD196. A. Clustering analysis of Th cell populations based on CD196 expression. B. Th cell cluster based on CD196 expression.

- **Fig. 5.** Clustering analysis of CD80 expression in CD4⁺ T cells. A. Clustering analysis of CD80 expression in CD4⁺ T cells. B. Clustering analysis of CD80 expression in CD4⁺ T cells.

- **Fig. 6.** Correlation of CD4⁺ T cell clusters with clinical outcomes after programmed death-ligand 1 (PD-1) blockade therapy. A. Correlation of CD4⁺ T cell clusters with clinical outcomes after PD-1 blockade therapy. B. Correlation of CD4⁺ T cell clusters with clinical outcomes after PD-1 blockade therapy.

Patients and Methods

This study included 60 consecutive patients who had histologically or cytologically confirmed stage IV or IIIIB-C non-small lung cancer (NSCLC) and were eligible for 1st line pembrolizumab therapy as a clinical practice from a single institution, Saitama Medical University International Medical Center, from March 2017 to November 2018. Fifty seven of 60 patients had TPS of 50% or greater. Peripheral blood samples for this study were collected after obtaining written informed consent and were analyzed by single cell RNA sequencing and a mass-spectrometer. The study protocol was approved by the Internal Review Board of Saitama Medical University.

Conclusion

We identified a novel Th cluster, Th7R, which is distinct from Th1 and Th17 with scRNAseq and CyTOF analyses.

Pre-treatment Th7R predicted antitumor efficacy with longer PFS and OS of PD-1 blockade therapy in two lung cancer validation cohorts.

Predictive potential on the immune status with Th7R from peripheral blood samples may pave the way for new personalized antitumor immunotherapy strategies for patients.

Disclosure

HK received honoraria from Ono Pharma, Chugai Pharma, AstraZeneca, BMS and grant/funding from Ono Pharma, Chugai Pharma, Boehringer Ingelheim, and Taiho Pharma.