Abstract 5342

Investigation of CD73 expression in response to immunotherapy in pan-cancer

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Background

- CD73, also known as NT5E, is a cell surface glycosylphosphatidlinositol-anchored glycoprotein, which can produce adenosine to inhibits anti-tumor immunity or immune evasion and leads to tumor growth and/or metastasis. Therefore, CD73 as a new immune checkpoint has attracted wide attention. However, there was few clinical study has explored the correlation between the expression of CD73 and the efficacy of PD-1 /L1 inhibitors.

Methods

- The data of 4751 patients with solid tumor from TCGA were used to analyze the correlation between NT5E and prognosis, and RNA-sequencing expression (level 3) profiles and corresponding clinical information for pan-cancer were downloaded from the TCGA dataset for Spearman correlation analysis of MSI/TMB/CD276 and NT5E gene expression. Immune score evaluation was conducted via immunedeconv R package. An independent cohort (the Hwang study cohort) with NT5E data from 20 patients with NSCLC, was used to analyze the prognostic effect of NT5E on PD-1 /L1 inhibitors.

Results

- In TCGA cohort, higher CD73/NT5E expression was associated with worse prognosis in 9 types of solid tumors, including HNSC, UVM, TGCT, STAD, LUAD, LUSC, PAAD and MESO, most independent of TMB/MSI status.
- It's a positive correlation between PD-L1 and NT5E expression in tumors (R=0.23,P<0.001), but a negative correlation in normal tissues (R=-0.19,P<0.001).
- However, the immune status of LUAD found that the TMB (P<0.001), MSI (P<0.001), and PD-L1 (P<0.001) in the high-expression NT5E group was significantly higher than low-expression group. Moreover, the expression of NT5E was significantly associated with high infiltration of B cells (P<0.001), but with low infiltration of M2 macrophages (P<0.01)and myeloid dendritic cells (P < 0.001). In Hwang study cohort, high CD73 expression had significantly better PFS (P=0.005; HR = 0.3; 95% CI, 0.11–0.84) after PD-1/L1 inhibitors in NSCLC patients.

Results

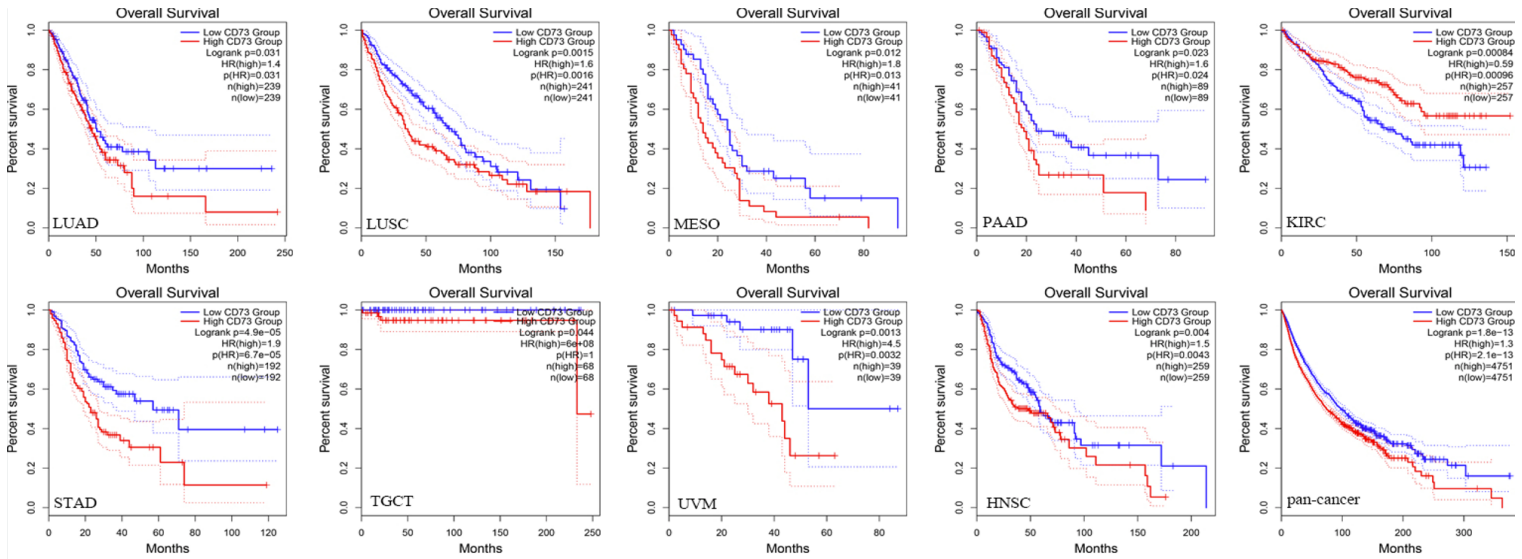

Figure1. Kaplan-Meier survival curves of OS in 9 types of solid tumors with high or low level CD73.

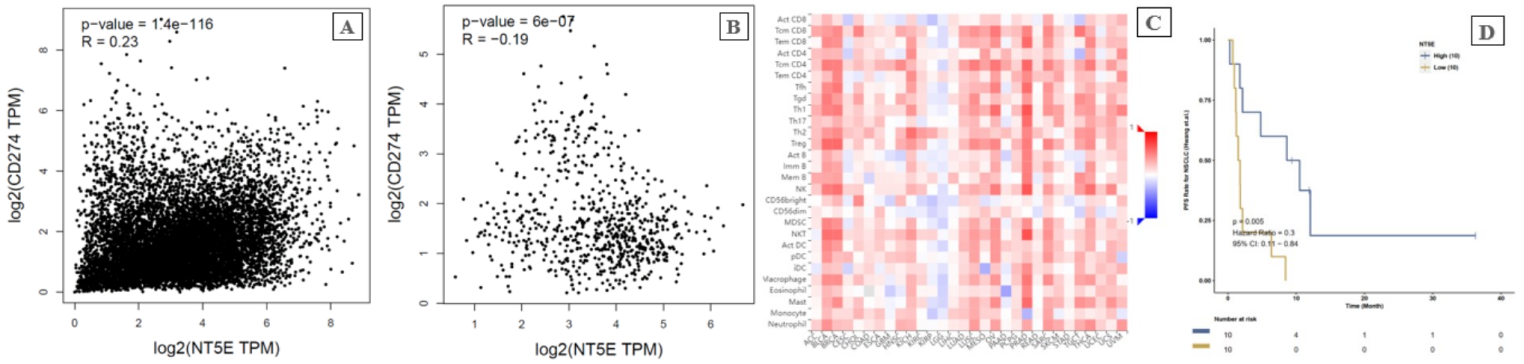

Figure2. A-B was the correlation between PD-L1 and NT5E in A）tumors and normal tissues. C was the heat map of immune microenvironment in solid tumors. D was the Kaplan-Meier survival curves of PFS in LUAD from Hwang cohort.

Conclusion

- Our results highlight the significance of CD73 as a potential target for cancer immunotherapy and as a promising biomarker for predicting ICI response in several tumors such as LUAD for its expression levels seem to be correlated with the status of immunotherapy-associated signatures.