Preexisting tumor host immunity delineates clinical outcomes in resectable NSCLC

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Background

- Neoadjuvant and adjuvant immune checkpoints blockade (ICB) have recently shown promising results in resectable NSCLC1,2. Yet, biomarkers that inform patient benefit with this approach remain largely unknown1. Here, we interrogated the tumor immune microenvironment (TIME) in early-stage NSCLC patients that underwent up-front surgery

Methods

- A total of 185 treatment-naïve early-stage NSCLC patients, that underwent curative surgical treatment between 2006 and 2018 at Hospital del Mar were included. None of the patients received adjuvant immunotherapy Table 1.

- Core biopsies from the surgical specimens were included in a tissue microarray. Immunohistochemistry of PD-L1, CD3, CD4, CD8, CD68, CD103 and FOXP3 were evaluated by digital image analysis (QuPath software) Figure 1.

- TIME was categorized into four groups using PD-L1 expression in tumor cells (<1% or ≥1%) and tumor infiltrating lymphocytes (TILs) based on intratumoral CD3 percentage (cut-off calculated using Youden’s index – 26.32%): 1) PD-L1/ TILs−, 2) PD-L1/TILs+, 3) PD-L1/CD3+, 4) PD-L1/CD3+. TIME patterns and immune markers were statistically compared on clinicopathological and molecular features and survival outcomes.

Results

- PD-L1/TILs+ tumors showed a reduced risk of relapse compared to PD-L1/TILs− (p=0.0471) Figure 2.

- PD-L1 +/TILs+ exhibit higher percentage of intratumoral CD8+ (cytotoxic T) positive cells compared with the other TIME groups (p<0.05) Figure 3A.

- Intrafraction FOXP3+ (regulatory T) positive cells were higher in PD-L1+TILs+ tumors (p=0.0109) Figure 3C.

- PD-L1 +/TILs+ tumors displayed a higher percentage of intratumoral CD103+ (tissue resident memory) positive cells (p<0.0001) Figure 3D.

- Intratumoral CD68+ (macrophages) positive cells were higher PD-L1+/TILs+ tumors (p=0.0055) compared with the other TIME groups Figure 3E.

Conclusions

- T cell subpopulations (CD103+, CD8+/FOXP3 ratio) exhibited by PD-L1+/TILs+ tumors suggest the potential role of ICB to revert the TIME towards a favorable immune context and thus, improve survival outcomes.

- Tumor immune microenvironment patterns based on tumor PD-L1 expression and the percentage of intratumoral CD3+ cells can be used as a tool for tailoring adjuvant strategies.

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References