Survival of non-small cell lung cancer patients predicted from expression of PD-L1, HLA class I and MICA/B on tumor cells

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Background: Several groups have reported that programmed death-1 (PD-1) ligand 1 (PD-L1) overexpression on tumor cells predicts a poor prognosis in patients with non-small cell lung cancer (NSCLC). Although recent studies have shown that PD-L1 overexpression on tumor cells predicts for improved clinical outcome in NSCLC patients treated with anti-PD-1/PD-L1 immunotherapy, PD-L1 low/negative tumors also benefit from anti-PD-1/PD-L1 immunotherapy. These findings suggest that study on multiple immune parameters should be considered. We recently reported that the overexpression of PD-L1 in tumor predicted a poor prognosis while overexpression of NK cell activating ligand MICA/B predicted improved clinical outcome in patients with resected NSCLC. It is well known that both T cell- and NK cell-mediated tumor recognition are influenced by HLA class I molecules. However, the roles of HLA class I molecules are different between T cells and NK cells; HLA class I T cell receptor immune synapse induces antigen-specific cytotoxicity by T cells, while HLA class I/killer cell immunoglobulin-like receptor synapse attenuates NK cell-mediated cytotoxicity. Here, we assessed the multiple immune parameters (PD-L1, MICA/B, and HLA class I) in NSCLC tissues to assess the prognostic factors in patients with resected NSCLC.

Methods: We examined resected tumor tissues from 91 patients with pathological stage IA-IIA NSCLC using immunohistochemical reaction for the expression of PD-L1, MICA/B, and HLA class I and then assessed whether the multiple immune parameters impact on the clinical outcome of patients with NSCLC.

Results: PD-L1low/MICA/Blow tumors have an excellent disease-free survival time (DFS) compared with PD-L1low/MICA/Blo w (p=0.010 by log-rank test) or PD-L1high/MICA/Blow tumors (p=0.035).

Conclusions: Multiple immune parameters using the expression status of MICA/B and PD-L1 or HLA class I on tumor cells are useful prognostic factors for NSCLC. We should have more concerns to NK cell-mediated tumor elimination in anti-PD-1/PD-L1 immunotherapy.

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