PD1/PD-L1 expression in NSCLC differs according to localisation, grading and subtype

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Aim: PD-L1 expression on tumor cells is supposed to reflect the immune-checkpoint of the receptor PD-1 on tumor infiltrating lymphocytes (TIL). Tumors may thus escape anti-tumor immune responses. To determine this relationship we investigated PD-L1 and PD1 expression in non-small cell lung cancer (NSCLC).

Methods: 484 lung cancer samples were subjected to PD-1/PD-L1 immunohistochemical double staining. Tumor expression of PD-L1 was recorded as membranous staining (H-score). PD-1 and PD-L1 expression on TIL was counted as absolute numbers of TIL per mm².

Results: Expression of PD-L1 was notably increased in sarcomatoid tumors (p < 0.001) compared with other NSCLC entities. 22.35% of adenocarcinomas (LAC; n = 179) compared with 31.16% of squamous cell carcinomas (SCC; n = 199) were positive for PD-L1 (p = 0.054). Across all NSCLC subentities, there was an association between histological tumor grade (G1-G4) and PD-L1 expression (p < 0.001). After stratification for tumor entity, this association remained significant for LAC (p < 0.001), only (SCC: p = 0.172). Surprisingly, TILs not only expressed PD-1, but more dominantly either PD-L1 or both PD-L1 and PD-1. PD-L1+ and PD-1+/PD-L1+ TILs showed strong association with general lymphocytic infiltration independent of location (p < 0.001), while PD-1+ TILs only had an association with lymphocytes located in the stroma (p < 0.001) (intraepithelial TILs; p = 0.194). Furthermore, we noted a significant correlation of TILs and membranous PD-L1 expression on tumor cells. Indicatively, there was a significant correlation between PD-L1+ TILs and PD-L1 expression on cancer cells. Intraepithelial PD-L1+ TILs (r = 0.551, p < 0.001) showed the strongest correlation. No similar correlation was present for PD-1+ TILs.

Conclusions: In a large NSCLC cohort we show that PD-L1 expression of tumor cells correlates with histological subtype and grading. The latter was most prominent in LAC. We also reveal a tight association between PD-L1 expression on NSCLC cells and TILs, especially intraepithelial PD-L1+ lymphocytes. We therefore suggest an autocrine/paracrine loop between NSCLC cells and TILs to be responsible for PD-L1 expression on either cell and thus giving rise to possible escape from anti-tumor inflammatory responses.

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