

P04.02 DIVERSITY OF CD4⁺ BLOOD T-CELL CLONALITY PREDICTS LONGER SURVIVAL WITH CTLA4 OR PD-1 CHECKPOINT INHIBITION IN ADVANCED MELANOMA

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Background T cells play a central role in tumor immunity. In principle, T cell requires antigen recognition by T-cell receptor (TCR) to gain effector function. Antigen-driven activation leads to clonal T-cell expansion with generation of progeny cells that all express the same chromotypic TCR. This makes TCR analysis a useful tool to comprehensively and individually understand antigen-specific T-cell responses. Indeed, we previously showed that the TCR repertoires of CD8⁺ T cells but not CD4⁺ T cells are restricted with many clones in the blood of psoriasis patients. Together with the strong genetic association to HLA-C*06:02 causing an autoimmune CD8⁺ T-cell response against melanocytes in psoriasis, our results from TCR analyses clearly indicate an autoimmune pathogenesis of psoriasis.

Patients and Methods Here, we utilize our expertise to understand how anti-tumor T-cell responses affect clinical responses and immune-related adverse events (irAEs) in therapeutic checkpoint inhibitions. We analyzed melanoma patients upon the therapeutic blockade of cytotoxic T-lymphocyte-associated protein 4 (CTLA4) or programmed cell death 1 (PD-1) using TCR Vβ-gene spectratyping.

Results Surprisingly, we observed variable levels of restriction in CD4⁺ and extensive restrictions in CD8⁺ T-cell repertoires in the blood of melanoma patients compared to healthy controls. This indicates the presence of a substantial numbers of CD4⁺ and CD8⁺ T-cell clones in the blood prior to the initiation of immunotherapy. The clones detected in the blood were enriched in tumor-infiltrating lymphocytes (TILs). This suggests that melanoma-reactive T-cell clones circulate more frequently in melanoma patients, although it is generally assumed that tumor-specific T-cell clones are only detectable in TILs. Greater diversification particularly in CD4⁺ blood T-cell clones before immunotherapy correlated with long-term survival after CTLA4 or PD-1 inhibition. In patients who developed severe immune-related adverse events (irAEs) during CTLA4 blockade, we detected newly expanded blood T-cell clones, suggesting that newly emerged T-cell responses contributed to these irAEs.

Conclusions Our data demonstrate that the diversity of T-cell clones in the circulation may reflect the anti-melanoma responses. This study provides a rationale for predicting clinical responses to checkpoint inhibitors using patient's blood, and also emphasizes importance of CD4⁺ T cell-mediated anti-tumor immunity in melanoma.

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P04.03 EXPRESSION PROFILES OF IMMUNE MARKERS AS PREDICTORS OF SURVIVAL IN SURGICALLY-TREATED NSCLC

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Background Surgery is the treatment of choice for early and for some locally advanced non-small cell lung cancer (NSCLC). Ipsilateral hilar and mediastinal lymph nodes are generally removed at the time of tumor resection. There is now increased awareness about the physiological role of lymph nodes in cancer. We investigated the expression profiles of immune-related markers in matched tumor tissue, affected and unaffected N1 and N2 lymph nodes in patients with NSCLC and their relation to survival.

Materials and Methods Internal hospital databases were screened for surgically-treated NSCLC patients with documented relapse or long-term disease-free survival (defined as 3 years). Data on patients' age, sex, surgery, (neo)adjuvant therapy, tumor characteristics and time and location of relapse was extracted. FFPE tissue blocks of primary tumor, affected and unaffected lymph nodes were collected. mRNA was extracted from these tissues and expression profiling of 751 immune-related genes was performed using the PanCancer IO 360 panel by NanoString Technologies. **Results**

A total of 754 NSCLC patients were screened. Of these, 71 patients showed long-term disease-free survival and 80 patients had local or systemic relapse within 3 years after surgery. Expression profiles of immune-related genes in tumor and lymph node immune populations differed between patients with and without 3-year disease-free survival.

Conclusions Expression profiles of immune-related genes differ between patients with and without relapse. Our findings show that differences in expression profiles of immune-related genes in tumor and lymph nodes should be taken into account when assessing patient prognosis.

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P04.04 PROGRAMMED DEATH-LIGAND 1 POSITRON EMISSION TOMOGRAPHY IMAGING DURING NEOADJUVANT (CHEMO)RADIOTHERAPY IN ESOPHAGEAL AND RECTAL CANCER (PETNEC): A PROSPECTIVE NON-RANDOMIZED OPEN-LABEL SINGLE-CENTER PILOT STUDY

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