

Conclusions The *in vitro* gene expression levels of individual chemokines (CXCL1 and CCL2) determines the MDSC infiltration *in vivo* into the TME. Targeting the chemokine-receptor axis of MDSC subpopulations could be a promising approach in the treatment of pancreatic cancer.

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P03.12 IMMUNOPHENOTYPING OF LIVER AND LUNG METASTASES IN COLORECTAL CANCER

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Background Immunotherapy is an attractive strategy for second-and further-line treatment of metastatic colorectal cancer (mCRC). However, currently immune checkpoint-inhibitors are limited to the small subgroup of dMMR-MSI-H patients. Therefore additional patient stratification markers for immunotherapy independent from the MSI-status are urgently required.

Materials and Methods In this study the immune infiltrate of 53 liver and 15 lung mCRC were immunohistochemically analysed and correlated with clinicopathological parameters related to the primary tumor and the metastatic lesion and the PD-L1 status. The CD3, CD8 and PD-1 infiltrate were quantitatively counted positive cells/mm² in three different topographic regions, namely invasion margin (IM), stromal (S) and intratumoral (IT). PD-L1 expression was semiquantitatively evaluated with the cut off > 1%. The statistical analyses were performed by the Fisher's exact-Test (two-tailed).

Results In liver metastases (LM) a high immune infiltrate of CD3 IM, CD3 S, CD8 S and PD-1 S, significantly correlated with an advanced stage (pN1/2; cM1) of the primary tumor. Independent of the type of adjuvant chemotherapy, a significantly higher fraction of CD3+ and CD8+ cells was found at the invasion margin of LM. In contrast, neoadjuvant chemotherapy induced a reduction of PD-L1 expression. Interestingly, a high CD8 IT infiltrate and a high PD-L1 expression correlated with KRAS wildtype. In addition, a high CD8 IT infiltrate and a high PD-L1 expression were found in confined LM, defined as less than two segments and unilobular distribution. A high PD-L1 expression was accompanied by a strong infiltrate of CD3, CD8 and PD-1 positive cells. In contrast, the small cohort of lung metastases showed a significant correlation for a high CD8 S infiltrate and a PD-1 IM infiltrate with right-sided metastases. Additionally, a high PD-1 IM infiltrate could be seen after neoadjuvant chemotherapy in lung metastases.

Conclusions Chemotherapeutic treatment strategy might have an impact on subsequent immunotherapy. Combination of anti-EGFR inhibitors with immunotherapy and CD3/PD-L1 Bispecific antibodies are promising options to treat liver and lung metastasis of CRC.

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P03.13 AGE-INDUCED CHANGES IN ANTI-TUMOR IMMUNITY ALTER THE TUMOR IMMUNE INFILTRATE AND REDUCE RESPONSE TO IMMUNE-ONCOLOGY TREATMENTS

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Background Immuno-Oncology research relies heavily on murine syngeneic tumor models. However, whilst the median age for a cancer diagnosis is 65 years or older, for practical purposes the majority of preclinical studies are conducted in young mice, despite the fact that ageing has been shown to have a significant impact on the immune response.

Materials and Methods Using aged mice bearing CT26 tumors, we analysed how aging impacts the immune composition of the tumor, spleen and tumor-draining lymph nodes by flow cytometry.

Results We found many age-related changes between aged (60–72 weeks old) and young (6–8 weeks old) mice, such as a reduction in the naïve T cell population and a decreased CD8/Treg ratio in aged animals. Profiling of co-inhibitory and co-stimulatory receptor expression levels on immune cells in aged versus young mice also identified altered expression profiles in both the periphery and tumor. We hypothesised that these differences may contribute to impaired anti-cancer immune responses in aged mice. To investigate this, we compared the anti-tumor efficacy of immune checkpoint blockade (PD-L1 and CTLA-4) and T-cell costimulation (OX-40) in aged versus young mice. Our data demonstrate that aged mice retained their capacity to generate effective anti-tumor immune responses, albeit often attenuated when compared to the responses observed in young mice.

Conclusions These differences highlight the potential importance of age-related immunological changes in assessing and refining the translational insights gained from preclinical mouse models.

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P03.14 PRECLINICAL CASE STUDY: PATIENT-DERIVED HEAD AND NECK CANCER XENOGRAFT ON MICE HUMANIZED WITH AUTOLOGOUS IMMUNE CELLS, A MODEL FOR PERSONALIZED IMMUNO-ONCOLOGY RESEARCH

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