pembrolizumab therapy and were correlated with response. Effector-type CNs enriched in tumor-infiltrating CD4+ T cells and dendritic cells were significantly increased after treatment in responders. In contrast, a regulatory T cell-enriched CN was significantly increased in non-responders before and after therapy. Furthermore, a spatial signature of cell-cell distances between tumor cells and effector/regulatory immune cells predicted therapy outcome. In addition, CIBERSORTx analysis revealed that tumor cells in responders, but not in non-responders, increased their expression of immune-activating genes.

Conclusions High-dimensional spatial analysis of CTCL tumors revealed a pre-existing immunosuppressive state in pembrolizumab non-responders. Thorough analysis of the TME therefore enables the discovery of novel spatial biomarkers in a concept that accounts for both cell type information and higher-order tumor architecture. Combining highly multiplexed microscopy with CIBERSORTx allows for the discovery of novel, predictive spatial biomarkers of immunotherapy response and will pave the way for future studies that functionally address these cell types and their interactions.

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On Demand Talk: ‘Lost in Translation’

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On Demand Talk: Young Researcher Session

05 DECONSTRUCTION OF HAMPERED DENDRITIC CELL DEVELOPMENT BY MICRO-ENVIRONMENTAL CROSS-TALK IN AN ORGANOTYPIC HUMAN MELANOMA-IN-SKIN MODEL

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Background Immune suppressive conditions in the melanoma tumor microenvironment (TME) block dendritic cell (DC) development and lead to the accumulation of M2-like macrophages and myeloid-derived suppressor cells (MDSCs). This will effectively hamper T cell priming, recruitment, and effector functions, and so interfere with the efficacy of immunotherapy. Targeting tumor-mediated myeloid suppression represents an interesting therapeutic option to promote the immune attack on tumors. The preclinical human models currently used to study myeloid suppression often fail to reflect the complexity of the TME.

Materials and Methods To study the cross-talk between melanoma and stroma cells and assess its effect on DC differentiation, we therefore established an in vitro three-dimensional (3D) reconstructed organotypic human melanoma-in-skin (Mel-RhS) model, allowing the monitoring of tumor growth and progression for up to six weeks.

Results Significantly higher levels of immune suppressive cytokines (IL-10, M-CSF, VEGF, TGFBeta) were detected in the melanoma model, constructed with the BRAF- and PTEN-mutated SK-MEL-28 cell line, as compared to its control (without melanoma cells). Indeed, Mel-RhS culture supernatants interfered with monocyte-to-DC differentiation, leading to the development of M2-like macrophages with a distinct phenotype (CD14+CD1aBDCA3+CD163+CD16+PD1L1+PD1L2+), as established by polychromatic flow cytometry. Correlation matrix heatmap analysis identified IL-10, TGF-beta and M-