Spatially resolving the cell-matrix architecture by Imaging Mass Cytometry

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Spatial mapping of the cell landscape in relation to the extracellular matrix (ECM) architecture has not been investigated in detail. Their co-localization is essential to comprehend the complexity of the tumor microenvironment (TME) potentially identifying critical TME relations impacting patient survival and therapy response. To decode the dynamic interplay between cell-ECM interactions, we developed a specialized Imaging Mass Cytometry (IMC)-based antibody panel targeting key cell types in combination with ECM components, facilitating comprehensive characterization of the TME. Our novel ECM antibody panel captures interstitial and basement membrane ECM subtypes, as well as localizing a subset of secreted molecules. Initially, we performed pseudo-cell analysis of the ECM sections of the whole tissue along with real cell segmentation using key cell markers. These segmentations were combined to generate an approximation map of co-localization of secreted soluble ECM molecules with structural ECM components and cell types. We further applied a fiber segmentation approach designed to accurately delineate fibrillar ECM structures within IMC datasets. This method enables detailed investigation of co-localization patterns between the structural ECM and soluble ECM molecules, such as chemokines, which are crucial for understanding immune cell recruitment and signaling within tumors. This approach allowed us to visualize and analyze the co-localization of netrin-1, collagens, and chemokines in a fresh-frozen clear cell renal cell carcinoma sample thereby determining the relation of ECM-anchored netrin-1/chemokine complexes with the TME. Using this unique IMC panel, unknown ECM protein complexes and their cell association have been identified.