University of Zurich[UZH]

Master Thesis in Quantitative Biology and Systems Biology

Characterization of Chemokine Expression in Metastatic Melanoma using Simultaneous Multiplexed mRNA and Protein Imaging by Mass Cytometry

Supervision

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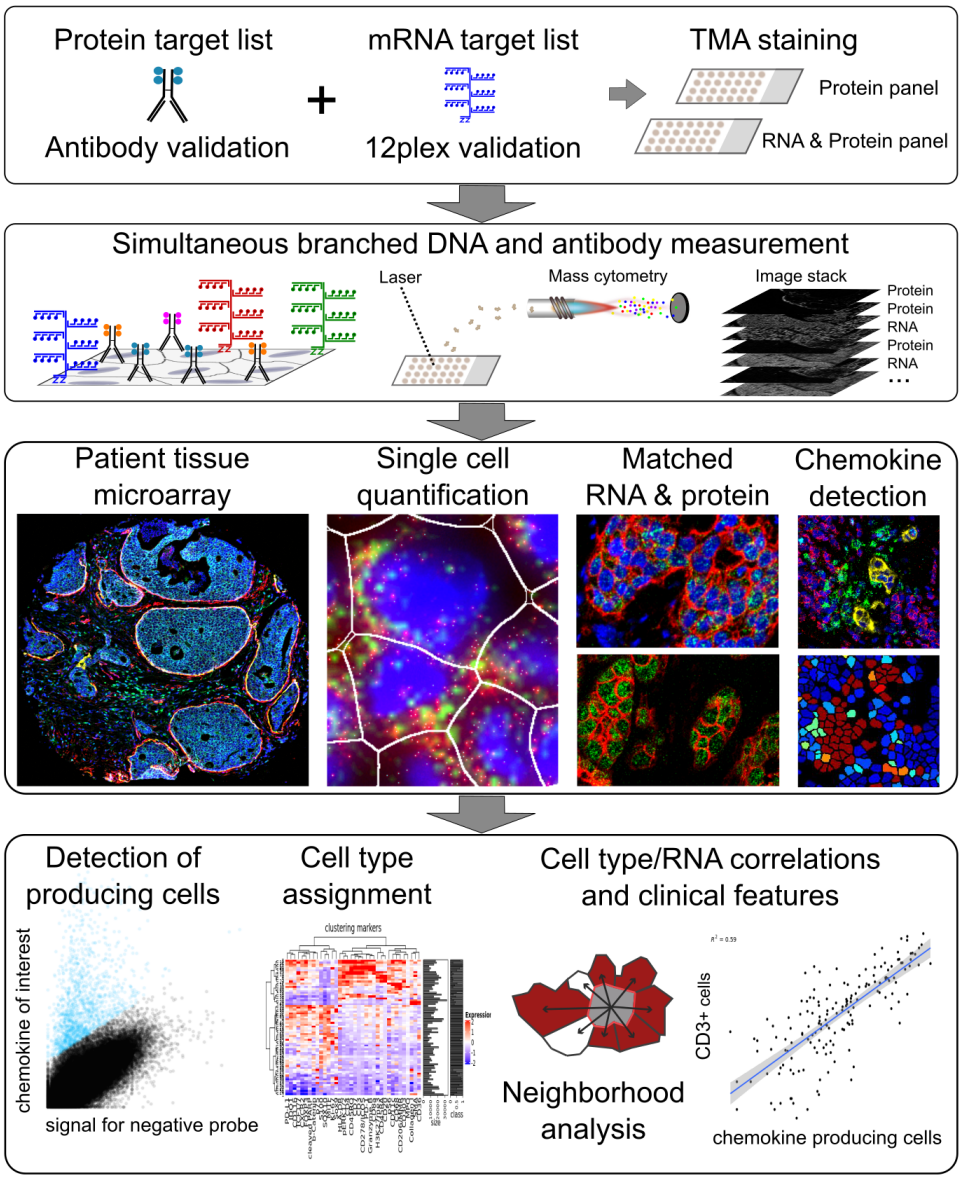
Abstract

Interactions between cancer and immune cells that shape the immune response against a tumor are a core component of cancer progression. Immune evasion and eventual disease progression is a complex biological phenomenon affecting the success of cancer treatment and patient outcome. Proteins of the chemokine family assume vital functions in immune cell migration, activation, and proliferation. The role of the chemokine family in the process of cancer progression has been studied in great detail but is not yet fully understood due to the many components of this complex system. Imaging mass cytometry, in combination with RNA in situ hybridization, allowed us to quantify the expression of chemokines and to identify the chemokine-producing cells. We extended the multiplexed detection of mRNA species by RNAScope^{TM} from 3 to 12 targets to analyze combinations of different chemokines and their co-localization with components of the tumor and its microenvironment. After a thorough validation of the system by assessing the unspecific binding of amplification trees, we applied the method to study chemokines and the immune system in a cancer tissue context. The analysis of 163 metastatic melanoma samples shed light on the characteristics of chemokine-producing cells and the relationship between chemokine-producing cells and immune infiltration patterns. We identified tumor cells as the primary source of *CXCL10* and *CXCL8* production and found that the expression of the T cell attractants *CXCL10* and *CXCL9* was insufficient to explain the full variability of the observed T cell infiltration, highlighting the complexity of the system. Our work provides an important basis for future mRNA imaging in mass cytometry and provides insight into the role of chemokines in metastatic melanoma.

Graphical Abstract



adapted from [62]