1. Spatial Phenotyping Reveals 13 Distinct Phenotypes in Recurrent and Metastatic Imaging

2. Cutaneous Squamous Cell Carcinoma (cSCC)

Cutaneous squamous cell carcinoma is the second most common non-melanoma skin cancer. Though prognoses are favorable in most cases, locally advanced and metastatic forms present an emerging health burden. Immunotherapy is a promising solution; however, resistance to immune checkpoint inhibitors (ICIs) warrants more research into tumor biology to identify predictors of response and resistance. To that end, we developed a novel antibody module of 10 metabolic and stress markers to further elucidate the tumor microenvironment in metastatic and recurrent cases.

3. Whole-slide Spatial Phenotyping of cSCC with Regional Lymph Node Metastasis Reveals an Immune-competent Microenvironment

3.1 Spatial Phenotyping Reveals 23 Distinct Cell Phenotypes in cSCC with Lymph Node Metastasis

3.2 Cellular Neighborhood (CN) Analysis Reveals 10 Unique Neighborhoods with High Immune Infiltration

3.3 Cellular Neighborhood Analysis reveals 10 unique spatial neighborhoods enriched in specific cell types and varying in abundance as shown in the legend. The accompanying bar chart (left) shows the percentage of each cell type (boxed as per the legend) in (a) within the CN. A Spatial Neighborhood Map (right) further illustrates the geographical distributions of the CNs across the entire tissue section. The extreme degree of immune infiltration in the tumor suggests an immune-responsive microenvironment that may produce a favorable response to immunotherapy.

4. Whole-slide Spatial Phenotyping of Recurrent and Metastatic cSCC Treated with Immunotherapy Reveals a Metabolically Active and Resistant Microenvironment

4.1 Spatial Phenotyping Reveals 13 Distinct Phenotypes in Recurrent and Metastatic cSCC

4.2 Deep Spatial Phenotyping based on Metabolic Markers Reveals High Metabolic Activity and Resistance to Oxidative Stress

5. The Value of Deep, Unbiased Spatial Analysis for Tumor-Immune Phenotyping

This study demonstrates the power of rapid, deep single-cell spatial phenotyping enabled by the PhenoCycler-Fusion system for a comprehensive analysis of the TME and tumor metabolism. Understanding differences in the tumor microenvironment at multiple levels—immunological, metabolic and stress—will be crucial for improving patient stratification and clinical care.