UNIQUE INSIGHTS INTO PDAC DEVELOPMENT REVEALED BY BOTH INSITUPLEX® AND IMAGING MASS CYTOMETRY

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Background Pancreatic cancer remains a deadly disease due to difficulties hindering its early diagnosis, giving way to metastasis of the tumor and resulting in poor prognosis. While there are many neoplasms of the pancreas, pancreatic invasive ductal adenocarcinoma (PDAC) is the most common and treatment options are few, with poor overall survival. Aggressive surgeries such as the Whipple procedure coupled to systemic chemotherapy is one of the few treatment options. Recently, several publications have demonstrated improved outcomes with the inclusion of immunotherapy to cytotoxic drug combinations in some patients, however optimally selecting patients as candidates for immunotherapy-chemotherapy combinations remains a critical challenge. The complexities of the tumor microenvironment have been implicated in the failure of chemotherapy, radiation therapy, and immunotherapy. The tumor microenvironment of PDAC is especially rich with multiple interactions between pancreatic epithelial/cancer cells, stromal cells, immune cells and the extracellular matrix (ECM). PDACs are characterized by a complex ECM of desmoplastic reaction consisting of an extensive and dense fibrotic stroma that surrounds and infiltrates clusters of malignant epithelial cells, together with the loss of basement membrane integrity and an abnormal vasculature.

Methods In the present study we demonstrate a tissue phenotyping workflow combining three complementary methods that can unravel novel insights in the complex tumor microenvironment. This novel translational workflow delivers tissue morphology information, spatial phenotyping of immune cell population on whole slides, and high dimensional imaging in selected regions of interest (ROI), by combining H&E, multiplex immunofluorescence (mIF), and Imaging Mass Cytometry (IMC™).

Results The use of the InSituPlex® UltiMapper® I/O PD-L1 kit enabled the streamlined combination and alignment of H&E and mIF data, leading to the strategic selection of relevant ROIs, while utility of IMC technology enabled downstream imaging of 35 protein markers associated with the ECM in the selected ROIs to provide a deeper understanding of the tumor microenvironment.

Conclusions The incorporation of advanced multiplex imaging platforms such as mIF and IMC with routine H&E workflow in tumor biology can deliver some of the much-needed insight into tumor morphology, cellular composition, cellular functions, and cell-cell interactions and paves the way for potentially improved clinical prognosis and efficacy prediction in patients with cancer.

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