CHARACTERIZATION OF THE TUMOR MICROENVIRONMENT IN PANCREATIC DUCTAL ADENOCARCINOMA USING MULTIPLEXED IMAGING


Background The pancreas is surrounded by highly vascularized organs such as the duodenum and the common bile duct. Pancreatic cancer often invades and metastasizes to these organs, and to more distant organs such as the liver, peritonium, lung, brain, kidney and bone. Conventional chemotherapy plus radiation, or in advanced disease chemotherapy plus targeted drug therapy can lengthen patient survival. However, even in patients that only have local disease, the 5-year survival rate is only around 40%, demonstrating that there is need for improved conventional and immune therapies for all pancreatic cancer patients. Tumor cells can evade treatments and continue to grow. Additionally, stromal cells in the tumor microenvironment are a critical support niche for continued tumor growth. Understanding all cells in the tumor microenvironment is essential for understanding tumor metastasis and improving cancer therapies, especially immunotherapies. In this study, dozens of biomarkers have been used to probe tumor heterogeneity in pancreatic ductal adenocarcinoma (PDAC) tissue. With Cell DIVETM multiplexed imaging, dozens of biomarkers can characterize cell heterogeneity, cellular activity and cell-to-cell spatial context within the TME.

Methods Sections were stained using conjugated antibodies (from multiple vendors) to various biomarkers in 4 channels plus DAPI and imaged using Cell DIVE. Multiple rounds of staining and imaging were accomplished using the Cell DIVE workflow (Leica Microsystems).

Results We examined the tumor, stromal compartment and immune cell contributions to the tumor microenvironment (TME). The panel enabled the examination of tumor associated stromal components and tumor infiltrating lymphocytes (TIL), angiogenesis, metastasis, invasion, inflammation, hypoxia, metabolism, and the immune response. We found that these heterogenous activities are often intertwined. For example, subregions within the tumor adapt to hypoxic conditions and can gain dominance by uncontrolled cell growth. Additionally, these hypoxic regions are devoid of immune cells.

Conclusions Taken together, multiplexed whole slide imaging enables spatially resolved tissue analysis of cellular activities in the TME, including new insights into cell-to-cell interactions and immune cell profile.

Ethics Approval Human samples were commercially available.