

B AND MYELOID CELL POPULATIONS DOMINATE IN THE METASTASIS COMPARED TO PRIMARY TUMORS OF PATIENTS WITH PANCREATIC CANCER

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Background Pancreatic ductal adenocarcinoma (PDAC) is a lethal malignancy with 5-year survival rate of only 11% for patients. To date, nominal data on the immune profile within metastatic PDAC of patients exists. Since most patients present with late-stage disease, defining the immunological landscape of metastatic disease could inform next-generation immunotherapy for PDAC patients.

Methods Using a 37-marker mass cytometry panel, freshly digested tumor tissue from surgically resected primary (n=6) and untreated liver punch biopsy metastatic (n=10) PDAC samples were evaluated for various immune features at the single cell level. Stained samples were fixed, run on a Helios™ mass cytometer and analyzed via FlowJo and Cytobank software.

Results Fewer CD45⁺ cells were present in metastatic compared to primary PDAC tumors. CD19⁺ B Cells (3.65% ± 5.19 of live cells) dominated among other immune populations in metastases. Yet these B cells appeared less activated in metastatic PDAC, signified by fewer B cells expressing HLA-DR⁺ (57.67% ± 26.49 of CD19⁺) versus the primary cohort (84.95% ± 21.19 of CD19⁺). Primary samples had significantly more myeloid, NK and T cells (p=0.017, p<0.01 and p=0.015, respectively) versus metastases. Moreover, primary tumors had significantly higher CD38⁺CD4⁺ and CD38⁺CD8⁺ T cells (consistent with an exhausted phenotype), while ICOS and TIGIT were elevated on T reg from primary vs. metastatic tumors. A survey of checkpoints revealed that LAG-3, TIGIT, and PD-1 were the most prevalent markers across both CD4⁺ and CD8⁺ T cells. Further analysis revealed proliferative (Ki67⁺) CD11b⁺ cells at both tumor sites. Metastatic sites had prevalent PMN-MDSC-like myeloid cells, but few M-MDSC-like myeloid cells. In-depth analysis of T cell populations revealed more CD4⁺Tbet⁺ Th1-like cells in primary (37.83% ± 34.13 of CD4⁺) as compared to metastatic samples (12.34% ± 31.43 of CD4⁺). Antigen-exposed CD45RO⁺PD-1⁺ T cells (CD4⁺: 60% ± 33.28; CD8⁺: 44.17% ± 23.38) and TCF-1⁺PD-1⁺CD8⁺T cells (37.88% ± 33.27 of CD8⁺) were also predominant in primary samples.

Conclusions These data indicate for the first time that metastatic PDAC is dominated by B and myeloid cells. While T cells were more evident in primary tumors, these cells harbored phenotypic properties of exhaustion. This work lays the foundation for a detailed spatial investigation into primary and metastatic PDAC tumors and could identify actionable targets to improve immunotherapy for PDAC patients.

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