cell-to-cell interactions were predicted between heterogeneous cell populations. Histologic inflammation was corroborated with scRNAseq and multiplex flow cytometry. Cell type-specific PD-L1 contributions within the TME were quantified using multispectral imaging.

Results Major cell type clusters (immune, epithelial, fibroblast and endothelial cells) were identified. Expression patterns for PD-1, TIGIT, LAG-3 and TIM-3 ligands were evaluated on these suppressive TME cell types. By modeling receptor-ligand interactions between CD8+ T cells and the rest of the major TME cell types, CD8+ T cells were predicted to form more ICR-ICL interactions with tumor-associated macrophages (TAMs) than with any other cell type. With focus on LGALS9/galectin-9 and CD274/PD-L1, flow cytometric analyses validated the scRNAseq observation that both ligands were expressed on TAMs from both inflamed and non-inflamed tumors. Furthermore, flow cytometry and multispectral imaging analyses implicated macrophages as one of the major contributors of CD274/PD-L1 within the TME.

Conclusions Our data suggest that in the setting of HNSCC, TAMs are one of the major contributors of ICL in the HNSCC TME. Strategies that selectively target this immunosuppressive population may be necessary to break tolerance to PD-1-targeting therapies.

Ethics Approval The study was approved by the UPMC Hillman Cancer's Ethics Board, approval number 99-069.

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Late-breaking abstracts

Biomarkers, immune monitoring, and novel technologies

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INTRATUMORAL DELIVERY CD40 AGONIST ANTIBODY VIA NOVEL NANOFLUIDIC DRUG-ELUTING SEED REDUCED TUMOR BURDEN OF MURINE PANCREATIC DUCTAL ADENOCARCINOMA

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Background Pancreatic adenocarcinoma (PDAC) is associated with extremely poor prognosis and a 5-year survival rate of 10% and remains a lethal malignancy. Surgical resection and combination with chemoradiotherapy are the current standard-of-care options, may improve long-term survival in localized disease; however, the majority of patients are diagnosed at advanced stage. The incorporation of immunotherapy in the treatment algorithm convenes a new era for PDAC treatment. Several immunotherapy approaches have been investigating for treating PDAC such as checkpoint inhibitors, vaccines, adoptive cell therapy, and so on. Immunotherapy has been shown as a promising therapeutic method for many cancer types; however, the complexity and immunosuppressive of the solid tumor microenvironment (TME) results in limited treatment efficacy for PDAC.

Methods To sensitize the TME in response to immunotherapy, we developed an implantable intratumoral drug delivery device, Nanofluidic Drug-Eluting Seed (NDES) can be injected via a minimally invasive trocar system that feasible for the clinical setting. NDES has shown efficiently delivered

immunotherapy to murine breast cancer model and reduced tumor burden and showed low liver inflammation compared to the intraperitoneal delivery approach in the previous study.¹

² Here, we utilized NDES for the sustained intratumoral delivery of the CD40 antibody. We compared the efficacy of NDES against intraperitoneal and intratumoral administration, which mimics conventional systemic treatment. Tumor growth was investigated for treatment efficacy. Local and systemic immune responses were assessed via flow cytometry.

Results NDES delivered CD40 significantly reduced tumor burden, some even achieved tumor clearance. Local NDES CD40 delivery approach showed a systemic increase of CD8+ and CD4+ T cells in the tumor-draining lymph node and spleen by flow cytometry. Furthermore, NDES CD40 treated mice showed an increase of CD8+ and CD4+ central memory T cells locally and systemically. We also investigated the combination with radiotherapy, no significant difference in tumor burden was observed when compared to single-agent CD40 antibody. The results indicated CD40 promotes TME response and improved treatment efficacy.

Conclusions These immunological responses demonstrate 'cold' to 'hot' tumor transformation, which translated to tumor burden reduction. Overall, NDES delivery strategy offers promise for enhancing therapeutic index and transforming the landscape of PDAC tumor therapy.

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IDENTIFICATION OF TUMOR ANTIGEN-SPECIFIC T CELLS IN THE PERIPHERAL BLOOD OF COLORECTAL CANCER PATIENTS

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Background Interactions between the immune system and the tumor are now recognized as key determinants of clinical outcome in colorectal cancer (CRC). Immune landscapes have been extensively studied within resected primary tumors and immune markers, such as T cells, have been found to be associated with CRC patients' survival. Little is known about the immune profile of cells in peripheral blood. We hypothesize that the functional status of T cells, characterized by their response to CRC tumor-associated antigens (TAAs), can be monitored in the peripheral blood of patients and that they have prognostic relevance in CRC.

Methods In vitro T cell responses to pools of overlapping peptides representing the TAAs MUC-1, hTERT, NY-ESO-1 and CEA were assessed by analyzing IFN-gamma and TNF-alpha production by CD8+ T cells using flow cytometry, in 5 stage II-III CRC patients just prior to surgical resection and 3 healthy age- and sex-matched controls.

Results T cells responding to MUC-1, hTERT, NY-ESO-1 and CEA were present in 3, 3, 1 and 5 CRC patients, respectively, whereas only one response to TAAs (MUC-1) was found in