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Uncovering and characterizing a biomarker in pancreatic cancer patients

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Less than 8% of patients with pancreatic cancer survive beyond five years due to inadequate early diagnosis and inadequate treatment options. Unfortunately, pancreatic cancer in general has not shown significant response to immune based checkpoint inhibitor as single or combination therapy to date. One reason may be the poor infiltration of pancreatic cancer by immune cells. To stimulate anti-pancreatic cancer cell immunity cancer vaccines have been developed. Our group performed a phase II clinical trial in which with resected pancreatic cancer who had received adjuvant chemotherapy +/- radiation therapy and who were still cancer free received an allogeneic, granulocyte-macrophage colony stimulating factor secreting pancreatic cancer vaccine. Using biosamples from these patients we developed a novel sereo-proteomics screen that uncovered pancreatic cancer biomarkers that correlated with improved survival (>3years) following vaccination. One of these biomarkers, myosin phosphatase target subunit one (MYPT1) shows strong expression in human and murine pancreatic ductal carcinoma compared to non-neoplastic ductal epithelium. We are correlating the expression of MYPT1 to the T-lymphocyte density and proximity to malignant cells. In addition, we developed MYPT1 deficient human pancreatic cancer cell lines using the CRISPR/CAS9 genome editing technique. The absence of MYPT1 alters the malignant potential of these cells compared to control cell lines. We conclude that biospecimens derived from patients with improved disease-free survival after cancer vaccine therapy can reveal biomarkers that appear to have function in malignant cell behavior.

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