Secretory Proteome of Pancreatic Cancer Reveals Elevation of Parkinson-Related Proteins

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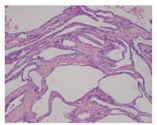
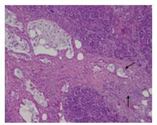
Introduction

Pancreatic Ductal Adenocarcinoma (PDAC) is the fourth leading cause of cancer death in USA and has the lowest survival rate for any solid cancer. This is largely due to late presentation by affected patients, thereby making therapeutic intervention difficult. The clinical standard used for diagnosis of PDAC CA19-9 is not specific for the cancer. Hence there is an urgent need to develop additional biomarkers that can aid in early diagnosis of PDAC. Also delineation of functional role of these markers in PDAC progression will reveal the pathways regulating aggressivity in these tumors. For this, we have generated preliminary data containing profiles of secretory proteins in PDAC using mass spectrometry and delineated the role of candidate protein in PDAC.

Histology of Pancreatic Pathology

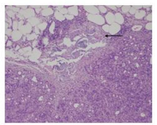


Benign Serous Microcystic Adenoma (100X) (H&E Stained Section)



Invasive Adenocarcinoma (100X) (H&E Stained Section)

Malignant glands with perineural invasion (arrows)



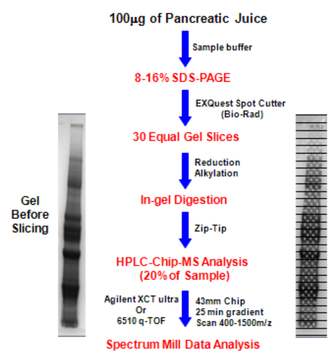
Benign Chronic Pancreatitis (100X) (H&E Stained Section)

Fat necrosis (arrow)

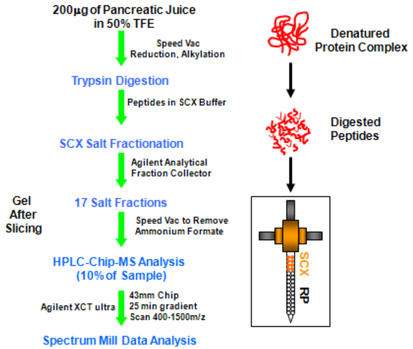
Experimental Workflow

Samples: 25 pancreatic duct fluids (juice) were collected during surgery into protease inhibitor containing tubes

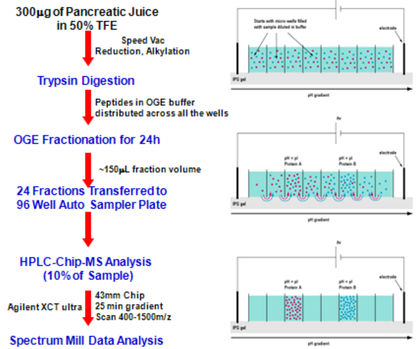
Method 1: 1D-Gel-LC-MS/MS



Method 2: Peptide SCX-LC-MS/MS



Method 3: Peptide OGE-LC-MS/MS



Results and Discussion

Figure 1 A

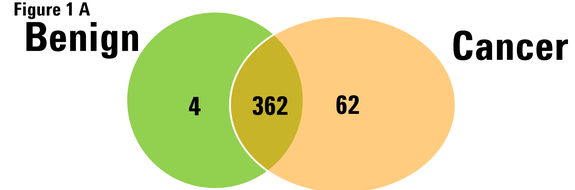
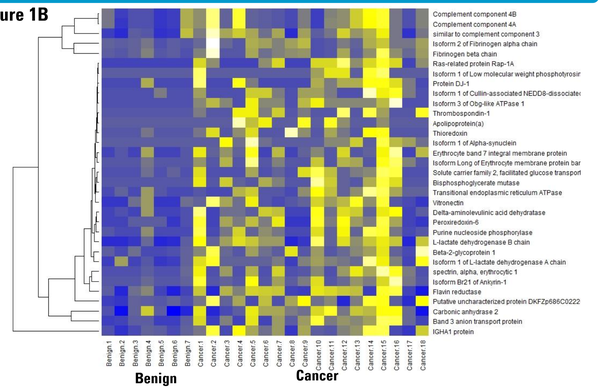


Figure 1A) Out of 428 differentially expressed proteins between cancer and benign group, 362 proteins were common to both whereas 4 and 62 proteins were unique to benign and cancer group respectively.

Figure 1B) Heat map of differentially expressed proteins in benign vs. pancreatic adenocarcinoma. Shades of yellow color shows high expression whereas shades of blue color shows reduced expression.

Figure 1B



Validation of Results

Figure 3

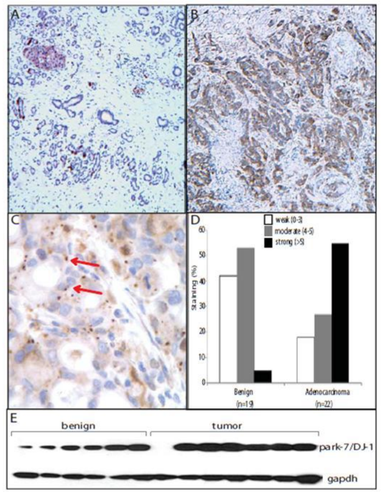


Figure 4

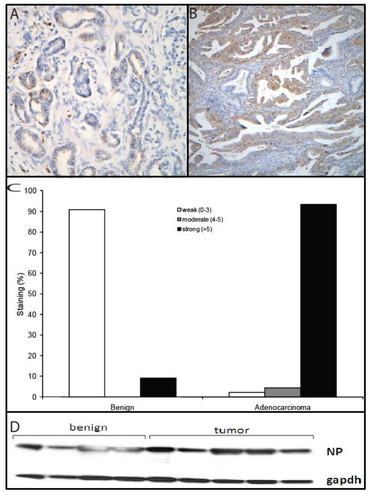


Figure 3 Tissue microarray analysis of synuclein A in pancreatic cancer and adjacent benign cancer. A) Immunostaining of adjacent benign pancreas B) Same as A but in pancreatic cancer C) Higher magnification of B showing SNCA granules. D) quantification of TMA staining in benign and PDAC samples (n=44). Magnification of A and B: 40X, for C: 100X E) PARK-7 protein expression (western blot) in PDAC-derived tissues.

Figure 4 Tissue microarray analysis of nucleoside phosphorylase (NP) in pancreatic cancer and adjacent benign cancer. A) Immunostaining of adjacent benign pancreas B) Same as A but in pancreatic cancer C) quantification of TMA staining in benign and PDAC samples (n=44). Magnification of A and B: 40X, for C: 100X D) NP protein expression (western blot) in PDAC-derived tissues.

Conclusions

- Pancreatic juice secretory protein profiles in PDAC using mass spectrometry identified candidate proteins in PDAC progression.
- Included among these were proteins known to be elevated in Parkinson's disease namely SNCA, PARK 7 and CAND1.
- Nucleoside phosphorylase was also highly
- Elevated in high grade PDAC.
- This is a novel finding indicative of a common nuance in development of Parkinson's disease and PDAC

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