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"Proteomics Analysis of PDAC and Pancreatitis Plasma Samples: Investigating Associations and Differences"

INTRODUCTION: Pancreatic cancer is currently the third-leading cause of cancer death in the United States. Roughly 90% of pancreatic cancer cases are pancreatic ductal adenocarcinomas (PDACs) and a vast majority present as advanced-stage with a 5-year survival rate of only 11%. Thus, early detection of pancreatic cancer is currently a crucial, yet challenging, goal. Having similar risk factors, pancreatitis has been associated with and is suggested to be an early manifestation or significant risk factor of PDAC. Therefore, comparisons between protein expression in PDAC and pancreatitis may lead to valuable insight into how the two are connected and the discovery of important biomarkers. Identified significantly expressed proteins and enriched pathways could be utilized or targeted in the diagnosis and treatment of pancreatic cancer.

METHODS: 30 human plasma samples from 3 different groups were randomized, prepared, and analyzed under standard protocol for extraction of proteins from plasma for peptide-based liquid chromatography-mass spectroscopy (LC-MS). 10 were collected from (1) a healthy control group with no diagnosis of pancreatitis or PDAC, 5 from (2) a group presenting with pancreatitis but no diagnosis of PDAC, and 15 from (3) a group diagnosed with PDAC. Label-Free Quantification (LFQ) intensity data collected from LC-MS for each sample group was processed and gap-filled using MaxQuant and Perseus. Pairwise comparisons (PDAC vs. Controls, PDAC vs. Pancreatitis, Pancreatitis vs. Controls) were performed using Student's T-Test to determine which proteins were significantly expressed across each pair. Significantly expressed proteins for each pair were mapped and analyzed using pathway enrichment analysis through Ingenuity Pathway Analysis (IPA) and Kyoto Encyclopedia of Genes and Genomes (KEGG).

RESULTS: LC-MS returned LFQ intensity data for 439 proteins across all 3 groups. Student's T-Test returned 27, 17, and 21 significantly expressed proteins that could be mapped on enriched pathways using IPA – between PDAC vs. Controls, PDAC vs. Pancreatitis, and Pancreatitis vs. Controls, respectively. Of the top 5 enriched pathways between PDAC vs. Controls and Pancreatitis vs. Controls, there were 4 common pathways, such as the Formation of Fibrin Clot (clotting cascade) pathway. The DHCR24 Signaling Pathway was also a top 5 canonical pathway between PDAC vs. Controls and the Extrinsic Prothrombin Activation Pathway between Pancreatitis vs. Controls.

CONCLUSIONS: As one of the leading causes of cancer deaths in the U.S., pancreatic cancer, mainly pancreatic ductal adenocarcinoma (PDAC), has a relatively low survival rate, which is only exacerbated by late diagnoses. Pancreatitis not only shares risk factors with PDAC but also may be an early indicator or risk factor for PDAC. In this study, LFQ-intensity data of plasma samples from healthy controls, pancreatitis patients, and PDAC patients were used to identify significantly expressed proteins and enriched pathways between sample groups. Further analysis of the identified significantly expressed proteins and enriched pathways may reveal potential biomarkers for early detection of PDAC by studying PDAC versus Pancreatitis.