

POSTER - PROTEINS AND PROTEOMICS

PROTEOMIC CHARACTERIZATION OF PLASMATIC EXOSOMES FROM PANCREATIC CANCER PATIENTS FOR DIAGNOSTIC AND PROGNOSTIC BIOMARKERS IDENTIFICATION

Mateus Aoki (mateus.aoki@fiocruz.br)

Anelis Maria Marin (anelis.marin@gmail.com)

Dalila Zanette (dalila.zanette@fiocruz.br)

Talita Helen Bombardelli Gomig (talitahbg@ufpr.br)

Alexandre Luiz Korte De Azevedo (alx.bio10@gmail.com)

Michel Batista (michel.batista@fiocruz.br)

Rodrigo Caldeira Brant (rodrigo.brant@fiocruz.br)

Pancreatic cancer is a significant global health issue, being the third leading cause of cancer-related deaths in the United States, and is predicted to become the second leading cause by 2030. The most common subtype, pancreatic ductal adenocarcinoma (PDAC), accounts for more than 85% of cases and is particularly concerning as half of patients present with metastatic disease at the time of diagnosis. Intraductal papillary mucinous neoplasm (IPMN) is a cystic neoplasm of the pancreas with benign characteristics that can potentially become malignant, and thus represent a significant diagnostic challenge. Current diagnostic methods for pancreatic cancer include the widely used biomarker carbohydrate antigen 19-9 (CA19-9), but it has limitations in terms of sensitivity and specificity. Imaging tests are also used, but they pose challenges

in terms of practical application and cost. The lack of reliable early prognostic and diagnostic methods and biomarkers is a major challenge in the management of pancreatic cancer. In this context, proteins play an essential role in the biological processes associated with cancer and have the potential to serve as reliable biomarkers. Therefore, this study aimed to investigate the proteomic landscape of plasma exosomes from patients diagnosed with PDAC and IPMN, compared to healthy controls (CT), in order to identify potential biomarkers with prognostic and diagnostic values. Additionally, the study aimed to understand the functional role of the exosome's proteome in pancreatic neoplasia. We isolated the plasma exosomes and analyzed its proteome by nano electrospray tandem mass spectrometry (nanoLC-MS/MS), and performed downstream statistical and bioinformatics analysis, using the Perseus (v. 6.2.2), MSigDB (v. 2023.1), STRING (v. 11.5), and NCG (v. 7.1) databases. A total of 319 differentially expressed proteins (DEPs) were identified among the exosome samples, but our analyses focused on the 135 proteins that were expressed in at least 70% of each group's samples to ensure their representative proteomes. Comparing PDAC and IPMN exosome proteomes to controls, we identified 24 and 33 differentially expressed proteins, respectively. Some of the most upregulated proteins in PDAC exosomes were CPN1, IGHV2-26, ITIH3, and CLU, while some of the most downregulated were C4BPB, APOB, CFH, and C1QB. In IPMN exosomes, KLKB1, LBP, CFB, and SERPINA1 were the most upregulated proteins while C5, APOD, C3, and C1QA were downregulated. In general, the protein-protein networks and enrichment analyses revealed interesting interaction clusters and pathways related to cancer development, such as the immune system, complement cascade, clotting-related and vesicle-mediated processes, regulation of insulin-like growth factor transport, platelet activation signaling, and G-protein signaling. Our analyses also highlighted candidate cancer drivers, including the upregulated IGLL, LBP, SERPINA1, SERPINA4, SERPING1, and the downregulated APOB, and C3, which were identified in these pathways and may have potential roles in pancreatic tumorigenesis. Overall, our study provides relevant insights into the proteomic landscape of plasma exosomes and their importance in pancreatic cancer. The DEPs identified in this study could serve as potential biomarkers for the early diagnosis and prognosis of PDAC and IPMN, which could ultimately lead to improved patient outcomes.