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PLASMA CELL-FREE RNA ANALYSIS HIGHLIGHTS KEY MOLECULAR CHANGES IN EARLY- AND ADVANCED-STAGE PANCREATIC CANCER

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Background : Cell-free RNA (cfRNA) analysis from plasma offers a unique window into the molecular alterations associated with pancreatic cancer. This study aimed to compare cfRNA profiles between pancreatic cancer patients and healthy controls to identify disease-specific RNA expression changes.

Methods : Plasma cfRNA was extracted from 34 pancreatic cancer patients and 8 healthy controls. Patients were classified into early-stage (n = 12; IA, IB, IIA) and advanced-stage (n = 22; IIB, III) groups. Differentially expressed genes (DEGs) were identified using thresholds of FDR < 0.05 and |Log2FC| > 0.5. Functional enrichment analyses were performed using Gene Ontology (GO), Reactome, and KEGG databases.

Results : In advanced-stage patients, 78 upregulated and 782 downregulated DEGs were identified compared to controls. Suppressed pathways included immune response (FDR < 0.001) and stimulus response (FDR < 0.001), with neutrophil degranulation notably downregulated (FDR < 0.005). Early-stage patients exhibited similar trends, with most DEGs overlapping those in the advanced stage. GO analysis highlighted significant enrichment in olfactory transduction (FDR < 0.01) and GPCR signaling (FDR < 0.01), while KEGG and Reactome analyses revealed neuroactive ligand-receptor interaction as an upregulated pathway (FDR < 0.01). Single-sample GSEA (ssGSEA) demonstrated downregulation of pancreatic progenitor cell-related genes ($p = 0.002$) and mild upregulation of α-cell genes ($p = 0.04$).

Conclusions : This study identifies immune suppression, GPCR and olfactory signaling, and cell-type-specific cfRNA alterations as key features of pancreatic cancer. These findings provide a basis for developing novel diagnostic and therapeutic strategies, warranting further validation.

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