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Poster Abstract Form

High-throughput plasma affinity proteomic profiling identifies a candidate biomarker to improve early-stage pancreatic ductal adenocarcinoma detection

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Introduction

Pancreatic ductal adenocarcinoma (PDAC) is the third leading cause of cancer-related death, with 13% 5-year survival [1,2]. No screening tests exist for PDAC, and diagnosis often occurs after disease progression [1]. This study explored the plasma proteome to identify biomarkers for early-stage PDAC detection.

Methods

Discovery cohort plasma from 19 patients with PDAC (stage I, n=8; II, n=7; III, n=4) and 30 controls was analysed for 5,416 proteins using Proximity Extension Assay technology [3] (Olink Explore-HT). Differentially expressed proteins (DEPs) were identified using one-way ANOVA post-hoc analysis (controls versus stage I, II or III; adjusted p-value<0.05). The top-ranked candidate was confirmed in the discovery cohort by enzyme-linked immunosorbent assay (ELISA), with positivity threshold determined using receiver operating characteristic (ROC) curve. Protein sensitivity was tested in a validation cohort (stage I, n=5; II, n=17; III, n=14; IV, n=19) and compared against CA19-9.

Results

368 DEPs were identified in PDAC versus controls, with fifteen shared across all stages. The most significantly upregulated DEP ("protein 1") was confirmed using ELISA in the discovery cohort. At a 362.5pg/mL threshold, it demonstrated 93.3% specificity and 78.9% sensitivity for all stages, and 80.0% sensitivity for early-stage (I/II). In the validation cohort, sensitivity was 94.5% for all stages and 90.9% for early-stage. CA19-9 had 72.7% sensitivity for all stages and only 45.5% for early-stage.

Conclusion

Protein 1 was highly upregulated in plasma from patients with PDAC and substantially improved early-stage sensitivity compared to CA19-9. Future work will validate this biomarker as a screening test for PDAC in a prospective cohort.

References

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2. Ushio, J., *et al.* Pancreatic Ductal Adenocarcinoma: Epidemiology and Risk Factors. *Diagnostics.* 2021.

3. Wik, L., *et al.* Proximity Extension Assay in Combination with Next-Generation Sequencing for High-throughput Proteome-wide Analysis. *Molecular & cellular proteomics*. 2021.