

Recent Advances in Biomarkers for Early Detection of Pancreatic Cancer

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DESCRIPTION

Pancreatic Cancer (PC) is one of the most lethal malignancies, characterized by late presentation, rapid progression, and limited therapeutic options. The majority of patients are diagnosed at advanced stages, when curative resection is no longer feasible, leading to a dismal five-year survival rate of less than 12%. Early detection remains the most promising strategy to improve outcomes, yet current diagnostic tools lack sufficient sensitivity and specificity. In recent years, significant progress has been made in the discovery and validation of novel biomarkers that could enable earlier detection of PC. These advances have the potential to transform clinical practice by identifying high-risk individuals and guiding timely interventions.

Biomarkers are measurable indicators of biological processes, disease states, or responses to treatment. In the context of PC, an ideal biomarker would allow non-invasive, cost-effective, and accurate detection of the disease at a stage when surgical resection is possible. The most widely used biomarker in PC is Carbohydrate Antigen 19-9 (CA19-9), which is elevated in the majority of patients. However, CA19-9 suffers from limitations including false positives in benign conditions such as pancreatitis and false negatives in patients who lack the Lewis antigen. Consequently, researchers have focused on identifying complementary or superior biomarkers to enhance diagnostic accuracy.

One area of recent progress is the use of circulating tumor DNA (ctDNA) as a liquid biopsy biomarker. ctDNA consists of fragmented genetic material released by tumor cells into the bloodstream. Studies have shown that ctDNA can detect common mutations in PC, particularly in the *KRAS* oncogene, which is mutated in over 90% of Pancreatic Ductal Adenocarcinomas (PDACs). The detection of *KRAS* mutations in plasma has demonstrated promise for early diagnosis and disease monitoring. Moreover, advances in next-generation sequencing (NGS) have improved the sensitivity of ctDNA assays, enabling detection of rare variants at low concentrations, which is critical for early-stage disease.

Exosomes and Extracellular Vesicles (EVs) have also gained attention as potential biomarkers. These nano-sized vesicles are

secreted by tumor cells and contain proteins, nucleic acids, and lipids reflective of their cell of origin. Exosome-derived biomarkers, such as glypican-1 (GPC1) and specific microRNAs (miRNAs), have shown potential in distinguishing PC patients from healthy individuals and those with benign pancreatic diseases. Exosome-based liquid biopsies are attractive due to their stability in circulation and the possibility of providing real-time insights into tumor biology.

Proteomics and metabolomics approaches have further expanded the biomarker landscape. High-throughput mass spectrometry has enabled the identification of unique protein signatures associated with early PC. For example, panels combining Thrombospondin-2 (THBS2) with CA19-9 have demonstrated improved sensitivity and specificity compared to CA19-9 alone. Similarly, metabolomic profiling of blood and urine samples has revealed altered metabolites linked to pancreatic tumor metabolism, such as changes in branched-chain amino acids and lipid metabolites. These signatures could complement traditional markers to improve early detection strategies.

Another area of promise is the integration of multi-analyte platforms. Combining ctDNA, exosomes, proteins, and metabolites into composite biomarker panels has been shown to outperform single biomarkers. For instance, multi-omics approaches can detect subtle molecular alterations that precede radiological evidence of disease, providing a critical window for intervention. Machine learning algorithms applied to large biomarker datasets further enhance predictive accuracy, moving toward precision diagnostics in PC.

Clinical application of these biomarkers is particularly relevant for high-risk populations, such as individuals with a strong family history of PC, hereditary cancer syndromes, or chronic pancreatitis. Surveillance programs incorporating novel biomarkers alongside imaging modalities like Endoscopic Ultrasound (EUS) and Magnetic Resonance Imaging (MRI) could significantly improve early detection in these groups. Several ongoing clinical trials are evaluating biomarker-based screening protocols, which may soon inform guidelines for early diagnosis.

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Despite these advances, challenges remain. Many candidate biomarkers require validation in large, prospective cohorts to confirm their clinical utility. Standardization of assay techniques, cost-effectiveness, and accessibility are additional barriers to widespread implementation. Furthermore, distinguishing PC from benign pancreatic conditions continues to be difficult, necessitating biomarker panels with high specificity. Nonetheless, the rapid pace of biomarker discovery and technological innovation provides optimism that these challenges can be overcome.

CONCLUSION

Recent advances in biomarkers for early detection of pancreatic cancer represent a critical step forward in addressing one of the

most lethal human malignancies. Liquid biopsy approaches using ctDNA and exosomes, proteomic and metabolomic signatures, and multi-omics integration are reshaping the landscape of PC diagnostics. While further validation and standardization are needed, these innovations hold the promise of shifting diagnosis to earlier, more treatable stages, ultimately improving survival and quality of life for patients. The era of biomarker-driven early detection in pancreatic cancer is approaching, bringing hope for a disease long considered untreatable in its late stages.