

Biomarkers For Early Pancreatic Cancer Detection

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Introduction

The critical need for early diagnostic biomarkers in pancreatic cancer is paramount to improving patient survival rates, as the disease is frequently identified at advanced stages where therapeutic interventions are significantly limited [1]. Research efforts are diligently focused on pinpointing specific molecules within accessible biological samples such as blood, urine, or tissue that possess the capability to detect pancreatic cancer in its nascent and most treatable phases. This multifaceted research landscape encompasses investigations into various classes of potential biomarkers, including protein-based markers, circulating tumor DNA (ctDNA), microRNAs (miRNAs), and metabolic alterations [1].

Circulating tumor DNA (ctDNA) has emerged as a particularly promising biomarker candidate for the early detection of pancreatic cancer, offering a non-invasive diagnostic avenue [2]. The analysis of ctDNA can effectively identify the specific genetic mutations that are characteristic of pancreatic cancer, thereby providing a crucial tool for early identification. Significant advancements in next-generation sequencing technologies are continually enhancing the sensitivity and specificity with which ctDNA can be detected, even when present at the extremely low concentrations typically found in early-stage disease [2].

MicroRNAs (miRNAs) represent another vital area of exploration for developing early diagnostic methods for pancreatic cancer [3]. Distinct miRNA profiles identified in serum samples have demonstrated a strong correlation with pancreatic ductal adenocarcinoma (PDAC). The inherent stability of miRNAs and their capacity for non-invasive detection render them highly attractive candidates for early diagnostic applications. Current research is concentrated on identifying robust miRNA signatures that can reliably differentiate PDAC from non-cancerous pancreatic conditions [3].

Protein biomarkers, with a particular focus on well-established markers like CA19-9 alongside novel protein panels, are also under rigorous investigation for their potential in early pancreatic cancer detection [4]. While CA19-9 has demonstrated utility, its limitations necessitate the development of combined protein panels to augment diagnostic accuracy. Ongoing research is employing proteomic approaches to identify a panel of proteins that can collectively enhance the sensitivity and specificity required for the early-stage detection of PDAC [4].

Given that metabolic reprogramming is a fundamental characteristic of cancer, research is actively examining metabolic biomarkers as potential indicators for the early detection of pancreatic cancer [5]. Subtle alterations in specific metabolites, such as amino acids or lipids, within bodily fluids can serve as early warning signs of PDAC. This metabolic profiling approach holds considerable promise for identifying unique metabolic signatures that are indicative of early-stage disease [5].

Extracellular vesicles (EVs) and their encapsulated cargo, including proteins and nucleic acids, are being evaluated for their utility as biomarkers in the early diag-

nosis of pancreatic cancer [6]. These EVs, which can transport disease-specific molecules, are readily detectable in easily accessible biofluids. The ongoing research in this domain aims to develop effective EV-based diagnostic assays that can improve both the early detection and subsequent monitoring of PDAC [6].

The integration of multiple biomarker modalities is recognized as an essential strategy for significantly enhancing the accuracy of early pancreatic cancer detection [7]. Current research is actively exploring the synergistic potential that arises from combining different types of biomarkers, such as ctDNA, miRNAs, and protein markers. This multi-omic approach is anticipated to yield superior sensitivity and specificity compared to tests relying on single analytes, ultimately leading to earlier and more dependable diagnoses [7].

Developing clinically applicable early diagnostic biomarkers for pancreatic cancer presents a series of challenges and necessitates a forward-looking perspective on future research directions [8]. Key obstacles include addressing tumor heterogeneity, achieving the high levels of sensitivity and specificity required for reliable early detection, and ensuring the cost-effectiveness of newly developed diagnostic tests. Future research is expected to heavily involve the advancement of liquid biopsy techniques, the application of sophisticated machine learning algorithms for data analysis, and the development of comprehensive multi-analyte panels [8].

Circulating tumor cells (CTCs) are being investigated for their potential as early diagnostic markers in pancreatic cancer [9]. CTCs, which are shed from primary tumors and enter the bloodstream, can offer valuable diagnostic and prognostic information. Significant progress in the techniques used for isolating and characterizing CTCs is making their analysis increasingly feasible and promising for integration into early detection strategies [9].

The tumor microenvironment (TME) is being explored as a potential source of early biomarkers for pancreatic cancer [10]. The immune cells, stromal components, and extracellular matrix within the TME can release specific signaling factors into the systemic circulation. A deeper understanding of these TME-derived signals may pave the way for the development of novel and effective early diagnostic approaches for pancreatic cancer [10].

Description

The imperative for early diagnostic biomarkers in pancreatic cancer is underscored by the disease's propensity for late-stage diagnosis, which severely curtails treatment options and diminishes patient outcomes [1]. Consequently, considerable research endeavors are directed towards identifying specific molecules present in easily accessible biological samples like blood, urine, or tissue that can facilitate the detection of cancer in its earliest, most treatable phases. This diverse research landscape encompasses the investigation of various potential biomarker categories, including protein-based markers, circulating tumor DNA (ctDNA), mi-

croRNAs (miRNAs), and metabolic alterations [1].

A significant focus within this field is the potential of circulating tumor DNA (ctDNA) as a highly promising biomarker for the early detection of pancreatic cancer, offering a non-invasive diagnostic approach [2]. The analysis of ctDNA enables the identification of specific genetic mutations characteristic of pancreatic cancer, thus providing a critical tool for early diagnosis. Concurrently, continuous advancements in next-generation sequencing technologies are significantly improving the sensitivity and specificity with which ctDNA can be detected, even at the very low concentrations typically found in early-stage disease [2].

MicroRNAs (miRNAs) have also emerged as another crucial avenue for developing early diagnostic methods for pancreatic cancer [3]. Specific miRNA profiles identified in serum samples have shown a strong association with pancreatic ductal adenocarcinoma (PDAC). The inherent stability of miRNAs and their accessibility through non-invasive sampling make them particularly attractive candidates for early diagnostic applications. Current research efforts are focused on identifying robust miRNA signatures capable of accurately differentiating PDAC from benign pancreatic conditions [3].

Protein biomarkers, including established markers like CA19-9 and novel protein panels, are subjects of ongoing rigorous investigation for their potential in early pancreatic cancer detection [4]. While CA19-9 has demonstrated some utility, its inherent limitations highlight the necessity for developing combined protein panels to enhance diagnostic accuracy. Current research is actively employing proteomic techniques to identify a panel of proteins that can collectively improve the sensitivity and specificity required for the early-stage detection of PDAC [4].

Recognizing that metabolic reprogramming is a fundamental hallmark of cancer, research is actively exploring metabolic biomarkers as potential indicators for the early detection of pancreatic cancer [5]. Subtle changes in specific metabolites, such as amino acids or lipids, within bodily fluids can serve as early warning signs of PDAC. This metabolic profiling approach holds considerable promise for identifying unique metabolic signatures that are characteristic of early-stage disease [5].

Extracellular vesicles (EVs) and their associated cargo, such as proteins and nucleic acids, are being systematically evaluated for their utility as biomarkers in the early diagnosis of pancreatic cancer [6]. These EVs, which can transport disease-specific molecules, are readily detectable in easily accessible biofluids. The research in this area aims to develop effective EV-based diagnostic assays that can improve both the early detection and subsequent monitoring of PDAC [6].

The integration of multiple biomarker modalities is widely recognized as an essential strategy for substantially enhancing the accuracy of early pancreatic cancer detection [7]. Current research is actively investigating the synergistic potential derived from combining various biomarker types, including ctDNA, miRNAs, and protein markers. This multi-omic approach is anticipated to achieve superior sensitivity and specificity compared to assays relying on single analytes, ultimately leading to earlier and more reliable diagnoses [7].

The development of clinically applicable early diagnostic biomarkers for pancreatic cancer is accompanied by a set of challenges and necessitates a forward-thinking perspective on future research directions [8]. Key obstacles include effectively addressing tumor heterogeneity, achieving the high levels of sensitivity and specificity crucial for reliable early detection, and ensuring the cost-effectiveness of novel diagnostic tests. Future research is expected to heavily involve advancements in liquid biopsy techniques, the application of sophisticated machine learning algorithms for data analysis, and the development of comprehensive multi-analyte panels [8].

Circulating tumor cells (CTCs) are under investigation for their potential utility as

early diagnostic markers in pancreatic cancer [9]. CTCs, shed from primary tumors into the bloodstream, can provide valuable diagnostic and prognostic information. Significant advancements in the techniques used for isolating and characterizing CTCs are making their analysis increasingly feasible and promising for incorporation into early detection strategies [9].

Furthermore, the tumor microenvironment (TME) is being explored as a potential source of early biomarkers for pancreatic cancer [10]. The immune cells, stromal components, and extracellular matrix within the TME can release specific signaling factors into the systemic circulation. A comprehensive understanding of these TME-derived signals may lead to the development of novel and effective early diagnostic approaches for pancreatic cancer [10].

Conclusion

Early detection of pancreatic cancer is critical due to late-stage diagnoses limiting treatment options. Research is actively exploring various biomarkers, including circulating tumor DNA (ctDNA), microRNAs (miRNAs), protein panels, and metabolic alterations, for their potential in identifying the disease in its earliest stages. Advances in technologies like next-generation sequencing are improving the sensitivity of ctDNA detection, while stable miRNA profiles and novel protein combinations are being investigated. Metabolic changes and extracellular vesicles (EVs) also show promise. Integrating multiple biomarker types through multi-omic approaches is seen as key to enhancing diagnostic accuracy. Challenges remain in addressing tumor heterogeneity and achieving high sensitivity and specificity. Circulating tumor cells (CTCs) and factors from the tumor microenvironment (TME) are also being explored as potential sources for early diagnostic markers.

Acknowledgement

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Conflict of Interest

None.

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