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Advances in Biomarkers for Pancreatic Cancer

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Abstract

Pancreatic cancer, a highly lethal digestive tract malignancy, has a 5-year survival rate below 10%, primarily due to late-stage diagnosis and limited therapeutic options. Over 80% of patients present with advanced disease, rendering them ineligible for curative surgery and facing a median survival of merely 6 months. Globally, pancreatic cancer ranks fourth in cancer-related mortality, with incidence nearly equaling mortality rates. Despite its clinical urgency, advancements in detection and treatment remain inadequate. Early diagnosis is pivotal to improving outcomes, as timely intervention may significantly prolong survival. This review synthesizes recent progress in identifying biomarkers for pancreatic cancer, emphasizing their potential to enhance early detection, guide therapeutic strategies, and ultimately reduce disease burden. Key findings highlight emerging biomarkers as critical tools for addressing this 21st-century oncological challenge.

Keywords

Pancreatic Cancer, Biomarkers, Early Diagnosis, Advances

1. Background of Pancreatic Malignant Tumors

Pancreatic cancer is a highly aggressive malignant tumor, mainly including pancreatic ductal adenocarcinoma (PDAC), pancreatic neuroendocrine tumors (PNETs), and other rare subtypes. Although the incidence of pancreatic cancer is relatively low, its mortality rate is extremely high, earning it the title of "silent killer". According to the 2022 GLOBOCAN statistics, the global annual new cases of pancreatic cancer are approximately 495,000, with nearly 466,000 deaths. The 5-year survival rate is less than 10%, ranking seventh among the causes of cancer deaths worldwide [1]. The extremely poor prognosis of pancreatic cancer mainly stems from the following aspects: First, early diagnosis is difficult. The pancreas is located deep within the body, and it lacks specific clinical symptoms, leading to most patients being diagnosed with locally advanced or metastatic disease. Statis-

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tics show that about 80% of pancreatic cancer patients are diagnosed with local or distant metastasis and are not eligible for radical surgery [2]. Additionally, although the widely used serum marker CA199 has some diagnostic value, its sensitivity and specificity are limited [3]. Second, the biological behavior is highly malignant. Pancreatic cancer is highly invasive and metastatic, capable of rapidly invading surrounding tissues, lymph nodes, and distant organs. Studies have shown that KRAS gene mutation is an early driver gene of PDAC, with over 90% of PDAC patients carrying KRAS gene mutations, along with mutations or inactivation of tumor suppressor genes such as TP53, CDKN2A, and SMAD4 [4]. These genetic alterations drive the uncontrolled proliferation and metastatic ability of pancreatic cancer cells. Resistance to existing treatments. The efficacy of traditional radiotherapy and chemotherapy for pancreatic cancer is limited. One reason is the presence of drug efflux pumps. Cancer cells overexpress ATP-binding cassette (ABC) transporters, such as P-gp (P-glycoprotein), to expel chemotherapy drugs from the cells, thereby reducing drug concentration [5]. Moreover, PDAC has a highly fibrotic tumor microenvironment. This dense matrix prevents immune cells (such as T cells and natural killer cells) from penetrating into the tumor core. This unique tumor microenvironment provides a protective barrier for the growth and drug resistance of pancreatic cancer, further restricting drug delivery and immune cell infiltration [6]. Early diagnosis, precise classification, and individualized treatment are key to improving the prognosis of pancreatic cancer patients, and the research on biomarkers is of great significance in these aspects.

2. Definition and Classification of Biomarkers

Biomarkers refer to molecules, cells, or specific characteristics that can be objectively measured and serve as indicators in normal biological processes, pathological biological processes, or therapeutic interventions. Pancreatic cancer biomarkers are typically used for diagnosis, staging, prognosis assessment, and prediction and monitoring of treatment efficacy. According to their functions and sources, pancreatic cancer biomarkers are mainly classified into the following categories: (1) Serum protein markers: identifying pancreatic cancer by detecting changes in serum protein concentrations, such as carbohydrate antigen (CA199). (2) Genetic markers: identifying pancreatic cancer by analyzing gene mutations, copy number variations, or gene expression patterns in tumor tissues or liquid biopsy samples. (3) Epigenetic markers: such as alterations in DNA methylation and histone modification patterns. (4) RNA markers: including long non-coding RNA (lncRNA) and microRNA (miRNA). (5) Metabolic markers: changes in pancreatic cancer-related metabolites. (6) Immune markers: markers related to immune cells in the tumor microenvironment.

3. Research Progress on Biomarkers for Pancreatic Cancer

3.1. Protein Markers

3.1.1. CA199

CA199 is currently the most widely used serum biomarker in the diagnosis and

monitoring of pancreatic cancer. However, its application has certain limitations. Studies have shown that the sensitivity of CA199 is 79% - 81%, and the specificity is 82% - 90%. It shows high diagnostic value in the detection of pancreatic cancer, but its use alone may be affected by other non-malignant diseases, such as biliary obstruction, chronic pancreatitis, and other systemic diseases, leading to false positive results [7]. Some patients may show elevated CA199 even without pancreatic cancer or pancreaticobiliary diseases, which may be related to individual differences (such as Lewis negative status) or other non-tumor pathological physiological changes [8]. Therefore, in clinical application, the trend of CA199 changes over time is more diagnostically significant than a single measurement, and it is necessary to combine the patient's imaging examination and clinical manifestations to comprehensively evaluate the cause. In the monitoring of pancreatic cancer recurrence, CA199 also plays an important role. Its level is closely related to the biological progression of the disease, and dynamic changes can serve as an early warning indicator of recurrence [3]. In summary, as a core biomarker for pancreatic cancer, CA199 requires dynamic monitoring of its changes and combination with other diagnostic methods to avoid misdiagnosis or overtreatment.

3.1.2. CA125

CA125 is a biomarker of great interest in pancreatic cancer research and plays a significant role in diagnosis, postoperative monitoring, and prognosis assessment. Studies have shown that the combined detection of CA125 with other markers (such as CA199 and CEA) can significantly improve the diagnostic sensitivity and specificity of pancreatic cancer, especially demonstrating high diagnostic value in early detection [9]. Moreover, the dynamic changes in CA125 levels after surgery are key indicators for evaluating the prognosis of pancreatic cancer patients. Patients with a significant decrease in CA125 after surgery usually have a better prognosis, while a continuous increase or insufficient decrease indicates a higher risk of recurrence [10]. In patients with pancreatic head cancer, CA125 has been confirmed as an independent prognostic marker, with high levels significantly associated with poorer survival rates. Even after adjusting for other variables, CA125 can effectively predict disease progression and recurrence risk in patients [11]. CA125 is not only a crucial tool for the diagnosis of pancreatic cancer but also holds significant clinical value in postoperative monitoring and individualized treatment decisions.

3.1.3. MUC1

Mucin-1 (MUC1) plays a significant role in the occurrence and development of pancreatic cancer and has considerable value in diagnosis, prognosis assessment, and treatment. Studies have shown that the expression level of MUC1 protein can serve as an independent prognostic marker for patients with pancreatic ductal adenocarcinoma. High expression of MUC1 is significantly associated with a poorer survival rate, while patients with low expression typically have a better prognosis [12]. Additionally, MUC1 enhances the chemoresistance of pancreatic cancer cells

by upregulating multidrug resistance-related genes (such as MDR1 and MRP2), leading to chemotherapy failure and an increased risk of recurrence, indicating its core role in the drug resistance mechanism [13]. Further research has developed a MUC1-specific monoclonal antibody-drug conjugate (HzMUC1-ADC), which has demonstrated significant anti-tumor effects in pancreatic cancer models, offering a potential new targeted treatment strategy for MUC1-positive pancreatic cancer patients [14]. Moreover, MUC1 regulates the metabolic pathways and chemoresistance of pancreatic cancer cells by activating the HIF-1α signaling axis. The activation of this pathway is closely related to tumor invasiveness and treatment failure, providing a new direction for reversing drug resistance [15].

3.2. Genetic Markers

3.2.1. KRAS Mutation

KRAS mutation is a core driver event in pancreatic cancer, with over 90% of patients carrying this mutation. It is detected at the early stage of pancreatic intraepithelial neoplasia, marking the occurrence and development of pancreatic cancer [16]. KRAS mutation continuously activates the MAPK and PI3K-AKT signaling pathways, promoting the proliferation, survival, and metastasis of tumor cells. Different KRAS mutation subtypes (such as G12D, G12V) have different impacts on clinical outcomes. Among them, the G12D mutation is associated with a worse survival rate [17]. Moreover, KRAS mutations often co-occur with TP53, CDKN2A, and other genes, and this synergistic effect not only exacerbates the formation of immunosuppressive tumor microenvironments but also reduces the response rate of patients to immunotherapy [17]. Although inhibitors targeting KRAS G12C mutations (such as sotorasib and adagrasib) show therapeutic potential in some patients, other KRAS subtypes still lack effective targeted drugs [18]. Studies have also shown that combination therapies (such as KRAS inhibitors combined with immune checkpoint inhibitors or chemotherapy) have significant advantages in overcoming treatment tolerance related to KRAS mutations, providing important directions for the optimization of future treatment strategies [18]. In summary, KRAS mutation is not only a key oncogenic event in PDAC but also a highly promising therapeutic target.

3.2.2. TP53 and SMAD4

Mutations in TP53 and SMAD4 exhibit a synergistic effect in PDAC, jointly exacerbating the tumor's invasiveness and metastatic potential. TP53 is the second most common mutated gene in PDAC, and its mutations are typically associated with genomic instability and increased tumor invasiveness [4]. Specifically, gain-of-function (GOF) mutations in TP53 enhance tumor cell proliferation, anti-apoptotic ability, and metastasis, significantly reducing patient survival rates [19]. SMAD4, as a key regulatory factor in the TGF-β signaling pathway, is frequently inactivated or lost in PDAC, closely related to tumor cell evasion of immune surveillance and microenvironment remodeling [4]. Studies have shown that the loss of SMAD4 can disrupt the tumor suppressive function of TGF-β signaling and

instead activate pro-tumor effects, thereby promoting tumor growth and metastasis [20]. These findings emphasize the importance of precise detection of TP53 and SMAD4 mutations and targeted therapy for their functional abnormalities.

3.2.3. BRCA Mutations

BRCA gene mutations have significant pathogenic and therapeutic implications in pancreatic cancer, especially in PDAC. Mutations in BRCA1 and BRCA2 interfere with the DNA damage repair mechanism, leading to genomic instability and promoting tumorigenesis [21]. A Mate study further demonstrated that BRCA mutations, particularly BRCA2, are significantly associated with a high risk of familial pancreatic cancer. Mutant carriers typically exhibit an earlier age of onset and unique tumor biological characteristics. This highlights the importance of incorporating BRCA testing into the screening of high-risk familial cases for early diagnosis [22]. In terms of treatment, PDAC patients with BRCA mutations show higher sensitivity to PARP inhibitors and platinum-based chemotherapy drugs, providing strong evidence for precision medicine [23]. However, the heterogeneity of treatment responses indicates that different BRCA mutation types may have distinct biological effects and clinical significance. These findings not only support the routine detection of BRCA mutations in pancreatic cancer management but also highlight the potential value of targeted therapeutic strategies in BRCA-related pancreatic cancer patients. Overall, BRCA mutations are both a key pathogenic factor in pancreatic cancer and an important research direction for personalized treatment and targeted drug development.

3.3. Epigenetic Markers

Epigenetics has played a significant role in the occurrence, development and treatment of pancreatic cancer, becoming a hot research field in recent years. Epigenetic alterations such as DNA methylation and histone modification are not only important characteristics of pancreatic cancer, but also have significant diagnostic and therapeutic value [24]. For instance, the expression of DNA methylation patterns in circulating tumor DNA (ctDNA) has been proven to have high sensitivity and specificity in the early diagnosis of pancreatic cancer, especially when combined with traditional markers such as CA199, the diagnostic accuracy is further improved [25]. Histone methylation also plays a key role in the proliferation, invasion and metastasis of pancreatic cancer cells. The overexpression of EZH2 is significantly associated with the malignancy of the tumor and the prognosis of patients, and therapeutic strategies targeting EZH2 are showing clinical potential [26]. In addition, the deletion of epigenetic regulators such as SIN3B can change the tumor microenvironment by regulating histone deacetylation, transforming immunosuppressive "cold tumors" into immunologically active "hot tumors", thereby enhancing the response of pancreatic cancer patients to immunotherapy [27]. At the same time, epigenetic modifications have also been proven to play a core role in cell plasticity and drug resistance formation, driving tumor heterogeneity and enhancing the resistance of cancer cells to drugs. Combined therapeutic

strategies targeting epigenetic modifications can help overcome drug resistance and inhibit recurrence [28]. Overall, these studies not only expand the understanding of the mechanism of pancreatic cancer occurrence, but also provide new directions and potential targets for early diagnosis and precise treatment.

3.4. RNA Markers

Non-coding RNA plays a key role in the occurrence and progression of pancreatic cancer, especially miRNA and lncRNA show significant effects in regulating tumor metabolism, immune escape and chemotherapy resistance. miRNA exerts tumor suppressor or promoting effects in pancreatic cancer cells by directly binding to target genes. For example, miR-505 effectively inhibits the glycolytic metabolism and tumor progression of pancreatic cancer by suppressing the expression of the glycolytic related gene HK2, but its expression is inhibited by the pro-cancer lncRNA LINC01448 [29]. Meanwhile, lncRNA has shown an important role in regulating the function of miRNA. lncRNA ANRIL significantly enhanced the chemoresistance of pancreatic cancer cells to gemcitabine by down-regulating the expression of miR-181a and activating HMGB1-induced autophagy [30]. Furthermore, studies have also shown that the synergistic effect of miRNA and lncRNA may promote immune escape and drug resistance in pancreatic cancer by regulating the tumor microenvironment [31]. miRNA and lncRNA in exosomes are regarded as important molecular markers, which can achieve non-invasive diagnosis and monitor disease progression in liquid biopsy, and provide new targets for treatment at the same time [32]. These studies not only reveal the core position of miRNA and lncRNA in the molecular mechanism of pancreatic cancer, but also indicate that targeting specific ncRNA pathways is expected to provide a brand-new strategy for the precise diagnosis and treatment of pancreatic cancer [33].

3.5. Metabolic Markers

In recent years, significant progress has been made in the application of metabolomics in the early diagnosis and differential diagnosis of pancreatic ductal adenocarcinoma (PDAC). Through large-scale metabolite analysis, researchers have identified a variety of metabolic biomarkers and their potential mechanisms closely related to the occurrence and progression of PDAC. First, for the differential diagnosis of PDAC and chronic pancreatitis, Mayerle *et al.* established a panel of nine metabolites, including amino acids, lipids, and other small molecules, using gas chromatography-mass spectrometry and liquid chromatography-tandem mass spectrometry. When combined with CA199, this panel significantly improved the ability to distinguish PDAC from chronic pancreatitis (AUC = 0.94). Among these metabolites, certain lipid derivatives were particularly effective in capturing disease-specific metabolic changes [34]. For the early detection of PDAC, Cao *et al.* identified isoleucine and adrenic acid as specific metabolic biomarkers and constructed a two-biomarker model (AUC = 0.93), which significantly outperformed the traditional CA199 detection method (AUC = 0.79). The

study also revealed 11 metabolic pathways that underwent significant changes in both the serum and tissues of patients with stage I PDAC [35]. Ren *et al.* further used untargeted metabolomics analysis in a multicenter study and found that metabolites such as prostaglandin, creatine, and palmitic acid were significantly upregulated in PDAC tissues and serum. The combination of these metabolites with CA199 significantly improved diagnostic performance (AUC = 0.949) [36]. Additionally, KRAS mutation is a molecular characteristic of PDAC. Liu *et al.* used single-cell mass spectrometry to identify 23 significantly different metabolites in KRAS-mutated pancreatic cancer cells, including organic nitrogen compounds, organic acids and their derivatives, and lipids. These metabolites revealed the mechanisms of KRAS-driven metabolic reprogramming and showed potential diagnostic value [37]. Finally, Weston *et al.* found in a longitudinal study that within 36 months prior to the onset of PDAC, patients experienced a significant decrease in visceral fat, subcutaneous fat, and serum lipid levels, while blood glucose levels gradually increased. These changes were already evident in the early stages of the disease, while the loss of muscle and bone tissue was concentrated within 6 months before diagnosis [38]. The exploration of PDAC metabolic biomarkers has provided a new direction for early detection. The combination of multiple metabolic biomarkers, especially in conjunction with the traditional tumor marker CA199, has shown significant clinical potential.

3.6. Immunological Markers

In recent years, immune biomarkers have demonstrated significant value in the diagnosis, prognosis, and treatment of pancreatic cancer, providing a new perspective for exploring its complex immune microenvironment. Non-coding RNAs (ncRNAs) carried by exosomes in liquid biopsies, such as miRNAs and lncRNAs, reflect the metabolic activities of tumor cells and the dynamic changes in the immune microenvironment. These ncRNAs can not only regulate the functions of key immune cells such as dendritic cells and macrophages but are also closely related to the progression of pancreatic cancer and the response to immunotherapy [32]. Additionally, the levels of tumor-infiltrating immune cells are also important markers. For example, high levels of CD8+ T cell infiltration are associated with better survival prognosis, while tumor-associated macrophages (TAMs) may promote immune suppression, leading to a poorer prognosis [39]. Immune checkpoint markers in the serum, such as soluble CD40 (sCD40), have also been shown to have potential applications in the diagnosis and treatment of pancreatic cancer. The level of sCD40 is positively correlated with tumor burden, can predict the efficacy of immunotherapy, and provides a basis for patient selection, further emphasizing its clinical significance [40]. Through integrative multi-omics analysis, pancreatic cancer can be classified into different immune subtypes, including the "inflammatory" subtype with high immune cell infiltration and expression of inflammatory factors, and the "cold tumor" subtype with significant immune suppression and poor response

to treatment. This classification of immune subtypes provides a theoretical basis for personalized treatment [41]. Immune biomarkers such as exosomal ncRNAs, levels of infiltrating immune cells, serum immune checkpoint molecules, and classification of immune subtypes all offer new ideas for the precise diagnosis and personalized treatment of pancreatic cancer. In the future, combining these biomarkers with clinical immunotherapy practices may significantly improve the prognosis and treatment outcomes for pancreatic cancer patients.

3.7. Circulating Tumor Cells (CTCs)

CTCs are cancer cells that have detached from the primary tumor and entered the bloodstream. They hold great potential as biomarkers for early detection, monitoring disease progression, and evaluating treatment efficacy. CTCs can be isolated from peripheral blood and analyzed for genetic mutations, protein expression, and other characteristics. Recent studies have shown that the presence and number of CTCs correlate with disease stage and prognosis in pancreatic cancer. Additionally, CTCs can be used to identify actionable mutations for targeted therapies, providing a liquid biopsy alternative to traditional tissue biopsies. Further research is needed to optimize CTC isolation and analysis techniques and to validate their clinical utility in pancreatic cancer management.

4. The Application of Biomarkers in Clinical Practice

4.1. Early Diagnosis

The early diagnosis of pancreatic cancer remains a key challenge, primarily due to the lack of reliable biomarkers with high sensitivity and specificity. Traditional serum biomarkers, such as CA199, although widely used in clinical practice, show significant limitations in the early stages of pancreatic ductal adenocarcinoma (PDAC), with low sensitivity and specificity [42]. To address these issues, research focus has gradually shifted towards the discovery of novel biomarkers, such as MUC16, THBS2, CEACAM5, and CA125. These biomarkers, when combined with CA199 to form a multimodal diagnostic panel, have demonstrated higher diagnostic accuracy [43]. In addition, advances in liquid biopsy-based technologies have made it possible to detect circulating tumor DNA, non-coding RNA, and salivary mRNA biomarkers (such as KRAS and CDKL3). These minimally invasive testing methods have shown significant potential in screening high-risk populations [44]. Proteomics and metabolomics analyses have further expanded the range of potential biomarkers, providing the possibility for discovering new molecular signatures that can enhance the effectiveness of early detection strategies [45]. Although emerging biomarkers hold promise, their clinical application is still limited by the need for large-scale validation studies to establish their diagnostic reliability and cost-effectiveness. Furthermore, integrating these biomarkers into a comprehensive diagnostic framework can overcome the limitations of single biomarkers, thereby significantly improving the early detection rate of PDAC and ultimately improving patient outcomes.

4.2. Prognostic Evaluation

Biomarkers are playing an increasingly important role in the prognostic assessment of pancreatic cancer, optimizing patient management strategies by providing insights into disease progression, survival outcomes, and potential therapeutic targets. Protein markers such as the S100 family (S100A2, S100A6, and S100P) have demonstrated significant prognostic value, with S100A2 being a strong predictor of survival after surgical resection (for example, patients negative for S100A2 have a better prognosis) [46]. Similarly, studies have identified epidermal protein glycosaminoglycan as a novel biomarker associated with poor prognosis, which functions by modulating the tumor microenvironment, suggesting its potential as both a prognostic marker and a therapeutic target [47]. In addition, gene markers such as LAMB3, FN1, KRT19, and ANXA1 have been shown to be highly significant, with FN1 and ANXA1 being closely related to immune cell infiltration and response to immunotherapy, highlighting their potential in guiding personalized treatment [48]. Moreover, recent advances in biomarker discovery have emphasized the integrated application of protein and gene markers to enhance predictive capabilities and drive the development of precision medicine [49]. Despite the significant potential of these markers in patient stratification and survival prediction, challenges remain. Variability of markers across different patient populations, limited reproducibility of research findings, and the lack of standardization in clinical application all limit their practical value. Additionally, the heterogeneity of pancreatic cancer increases the difficulty of identifying markers with universal reliability. Nevertheless, the integration of multi-omics approaches and advancements in bioinformatics hold promise to overcome current barriers and provide more robust and personalized prognostic assessment tools for pancreatic cancer management.

4.3. Personalized Treatment

In recent years, the role of biomarkers in advancing personalized treatment for pancreatic cancer has garnered increasing attention. Biomarkers provide key insights into tumor biology, making it possible to develop customized treatment strategies tailored to individual patients. For instance, molecular profiling has been recognized as essential for optimizing therapeutic efficacy, with targeted therapies significantly improving patient outcomes based on specific molecular characteristics [50]. In resectable pancreatic cancer, predictive markers such as hENT1 and SPARC have shown potential in guiding the selection of chemotherapy and radiotherapy, although their clinical utility still requires further validation [51]. Moreover, advances in mRNA vaccine technology have introduced new possibilities for personalized treatment. By targeting patient-specific tumor antigens and eliciting robust immune responses, this approach represents a novel therapeutic strategy compared to traditional cancer vaccines [52]. In advanced pancreatic cancer, molecular profiling has facilitated the application of matched targeted therapies, demonstrating potential for improving clinical outcomes and further proving the

feasibility of precision medicine in this field [53]. Despite these significant advancements, challenges remain in integrating biomarkers into clinical practice. Although they hold great potential for optimizing treatment strategies and improving survival rates, issues such as the heterogeneity of pancreatic tumors, the high cost of molecular profiling, and insufficient validation of biomarkers limit their widespread application. Therefore, while biomarkers offer promising avenues for advancing personalized treatment for pancreatic cancer, continued research and clinical validation are needed to overcome these limitations and fully realize their potential.

5. Outlook and Challenges for the Future

Biomarkers have demonstrated significant potential in the early diagnosis, prognostic assessment, and personalized treatment of pancreatic cancer, offering important opportunities to improve patient survival rates and optimize therapeutic strategies. However, their clinical application still faces numerous challenges. In the future, with the continuous development of multi-omics technologies (such as genomics, proteomics, and metabolomics), the discovery and validation of pancreatic cancer-related biomarkers will become more precise, potentially enabling more personalized and precise medical care. However, the marked heterogeneity and complexity of pancreatic cancer remain the main obstacles in biomarker research. The diversity of the tumor microenvironment, molecular characteristics, and treatment responses among different patients makes the development of universal biomarkers difficult. In addition, clinical translation still needs to overcome some key issues, including the standardization of biomarker detection, further improvement of sensitivity and specificity, and insufficient cross-institutional validation. One of the primary challenges in translating biomarker research to clinical practice is the lack of standardized detection methods. Biomarker assays must be reliable, reproducible, and consistent across different laboratories and clinical settings. However, variations in sample collection, processing, and analysis techniques can lead to significant discrepancies in results. For example, the detection of circulating tumor cells (CTCs) and circulating tumor DNA (ctDNA) requires highly sensitive and specific methods, but current techniques vary widely in their efficiency and accuracy. Similarly, the analysis of epigenetic markers such as DNA methylation and histone modifications can be influenced by the choice of detection platform and the interpretation of results. To address this challenge, there is a need for standardized protocols and guidelines for biomarker detection. This includes establishing uniform procedures for sample collection, processing, and storage, as well as validating detection methods across multiple centers. The development of reference materials and quality control standards can also help ensure the consistency and reliability of biomarker assays. Economic costs and technical accessibility may also limit their application in resource-limited areas. Future research needs to strengthen multi-center collaboration, combined with artificial intelligence and big data analysis, to optimize the biomarker screening pro-

cess. At the same time, integrating biomarkers with novel therapeutic strategies (such as immunotherapy and targeted therapy) holds promise for further improving the treatment outcomes of pancreatic cancer. In summary, although biomarkers have shown promise in pancreatic cancer research, their comprehensive translation into clinical applications still requires addressing complex scientific and technical challenges. Only through continuous basic research and clinical validation, as well as multidisciplinary collaboration, can the true potential of biomarkers in the diagnosis and treatment of pancreatic cancer be realized.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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