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Pancreatic Cancer: A Functional and Clinical Proteomic Investigation

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Abstract

One of the most fatal forms of cancer is pancreatic ductal adenocarcinoma, with a median survival time of less than six months. PDAC patients have few therapeutic options, and surgery is still the most effective treatment, so early diagnosis is critical. The desmoplastic reaction of its stroma microenvironment, which actively interacts with cancer cells to orchestrate crucial aspects of tumorigenesis, metastasis, and chemoresistance, is one characteristic of PDAC. To decipher PDAC biology and develop intervention strategies, it is essential to conduct global research on cancer-stroma crosstalk. The rapid advancement of proteomics technologies over the past ten years has made it possible to profile proteins, post-translational modifications, and their protein complexes with an unprecedented level of dimensionality and sensitivity. Here, beginning with our ongoing comprehension of PDAC qualities, including forerunner sores, movement models, growth microenvironment, and remedial headways, we depict how proteomics adds to the utilitarian and clinical investigation of PDAC, giving experiences into PDAC carcinogenesis, movement, and chemoresistance. We sum up late accomplishments empowered by proteomics to efficiently examine PTMs-intervened intracellular motioning in PDAC, disease stroma collaborations, and potential helpful targets uncovered by these practical examinations.

Keywords: Proteomics • Clinical proteomics • Protein profiling • Biomarkers

Introduction

Pancreatic ductal adenocarcinoma, which comprises a majority of pancreatic cancers, is one of the most lethal diseases with a median survival time of less than 6 months. With limited therapeutic options, PDAC is likely to become the second leading cause of cancer-related mortality by 2040. As specific symptoms are rarely exhibited and clinically used biomarkers lack enough sensitivity and specificity for early detection, approximately 80% of tumors are detected at metastatic stages and are not surgically resectable; for patients who receive surgical resection and subsequent adjuvant therapy, a majority will relapse. Current cytotoxic chemotherapies, such as FOLFIRINOX and gemcitabine, only extend patient survival in the range of months, and the development of targeted therapies for PDAC is extremely challenging due to complicated tumor heterogeneities. A prominent pathological characteristic of PDAC is the typical desmoplastic reaction of the tumor microenvironment, which is due to the deposition of extracellular matrix by the highly abundant cancer-associated fibroblasts in the TME, which occupy the majority of the tumor mass. This highly fibrotic TME and multilayered interplay with cancer cells pose a barrier for preventing the infiltration of drugs. Due to the heterogeneity of different stroma subpopulations, deconstructing the stroma contents has been shown to have controversial effects on either inhibiting or promoting tumor progression. Thus, systematically exploring the heterogeneity of stromal cells and their functional crosstalk with cancer cells is critical for improving the understanding of their tumor-supportive and tumor-suppressive capacity, and facilitating the development of early diagnostic biomarkers and effective targeted therapies.

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Description

Extensive efforts have been made to study the genomic and transcriptomic landscapes of PDAC and provide insight into mutational mechanisms, molecular subtypes, and potential therapeutic targets for precise treatments. Characterizing genetic changes alone is insufficient to interpret disease occurrence and development, including in PDAC. Proteins are the direct building blocks of biological processes, and they are major drug targets. Mass spectrometry based proteomics is essential to bridge the gap between PDAC phenotype and genotype [1]. Over the past years, dramatically improved proteomic technologies and analytical platforms have enabled global profiling of proteins, post-translational modifications, and their protein complexes at unprecedented sensitivity and dimensionality. Here, we first provide a brief introduction of our current understanding of PDAC characteristics, including precursor lesions, progression models, the tumor microenvironment, and therapeutic advancements. Then, we describe how proteomics contributes to the functional and clinical exploration of PDAC, providing insights into PDAC carcinogenesis, progression, and chemoresistance. We summarize recent achievements enabled by proteomics to systematically investigate PTMs-mediated intracellular signaling in PDAC, cancer-stroma interactions, and potential therapeutic targets revealed by these functional studies [2].

We also highlight proteomic profiling of clinical tissue and plasma samples to discover and verify useful biomarkers that can aid in the early detection and molecular classification of patients. In addition, we introduce spatial proteomic technology and its applications in PDAC for deconvolving tumor heterogeneity. Finally, we discuss future prospects of applying new proteomic technologies in comprehensively understanding PDAC heterogeneity and intercellular signaling networks. Importantly, we expect advances in clinical functional proteomics for exploring cancer biology directly by high-sensitivity functional proteomic approaches starting from clinical samples [3].

Due to their late diagnosis, PDAC patients frequently have poorer prognoses than those with other types of cancer. The following are the results of a quantitative analysis of the genetic evolution trajectory of pancreatic cancer metastases: it requires no less than a decade from the event of beginning transformation to the introduction of the originator cell; The onset of metastasis may take at least five more years; Between metastasis and death, approximately two years may pass. Only about 10% of PDAC patients have a tendency to develop malignant tumors in their reproductive systems, and the majority of people only experience somatic progression of ductal epithelium alterations [4].

Somatic mutations in driver genes, such as point mutations, frequently occur in four primary driving genes in primary PDAC tumors. KRAS mutations occur in some normal ductal epithelial cells and almost all low-grade pancreatic intraepithelial neoplasias during the progression of PDAC. High-grade PanINs are more likely to contain mutations in tumor suppressor genes like CDKN2A, while the highest-grade lesions are accompanied by TP53 and SMAD4 loss. However, the biological and clinical differences between PDAC tumors cannot be fully explained by somatic mutation alone. Some histologically normal ductal epithelium frequently share somatic mutations that are similar to PDAC. Patients with chronic pancreatitis have also been found to have the most common somatic mutation, KRAS. Truth be told, patients with persistent pancreatitis are at an expanded gamble of PDAC contrasted and those not. Because of their likenesses in clinical, radiological, and biochemical nature, misclassification of PDAC as constant pancreatitis has likewise prompted a terrible guess. PDAC heterogeneity necessitates systematic investigation of numerous additional factors [5].

Conclusion

Although MS-based proteomics still faces low sensitivity and throughput compared with transcriptomic analysis based on advanced sequencing technologies, it is widely recognized as an indispensable and powerful tool to discover biomarkers and elucidate molecular mechanisms by quantitatively measuring proteins, PTMs, and their associated protein complexes on a large scale. As described in this review, many achievements have been made by the application of proteomics in functional and clinical research on PDAC, a dreadful disease with limited therapeutic options. Examples include combinatory functional proteome profiling to interpret tumor-stroma interactions and nominate therapeutic targets, spatial proteomics to interpret PDAC tumor heterogeneity, and plasma proteome profiling to identify diagnostic and prognostic biomarkers for PDAC, especially by isolation of exosomes to increase the specificity of biomarker candidates. Further clinical translation of these proteomic discoveries will require a high level of expertise across multiple disciplines, including technology development, medical oncology, pathology and clinical trials.

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Conflict of Interest

None.

References

1. Rahib, Lola, Benjamin D. Smith and Rhonda Aizenberg. "Projecting cancer incidence and deaths to 2030: The unexpected."
2. McGuigan, Andrew, Paul Kelly, Richard C and Turkington, et al. "Pancreatic cancer: A review of clinical diagnosis, epidemiology, treatment and outcomes." *World J Gastroenterol* 24 (2018): 4846.
3. Kamisawa, Terumi, Laura D. Wood, Takao Itoi and Kyoichi Takaori. "Pancreatic cancer." *The Lancet* 388 (2016): 73-85.
4. Anderson, Leigh. "Candidate-based proteomics in the search for biomarkers of cardiovascular disease." *Physiol J* 563 (2005): 23-60.
5. Burris, HA 3rd, Malcolm J. Moore, John Andersen and Mark R. Green, et al. "Improvements in survival and clinical benefit with gemcitabine as first-line therapy for patients with advanced pancreas cancer: A randomized trial." *Clin Oncol* 15 (1997): 2403-2413.

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