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Proteomics in Pancreatic Ductal Adenocarcinoma: Current Advances and Translational Perspectives

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ABSTRACT

Background: Pancreatic ductal adenocarcinoma (PDAC) remains one of the most lethal malignancies, with a median overall survival below one year in most clinical settings and limited options for early detection. Although comprehensive genomic profiling has established the dominant mutational landscape, including near-universal KRAS alterations and frequent alterations in TP53, CDKN2A and SMAD4, tumour phenotypes are ultimately executed at the protein level. Mass spectrometry-based proteomics has therefore become a central platform for PDAC research, enabling quantitative assessment of signalling pathway activity, characterisation of the tumour microenvironment, and identification of circulating biomarkers that may reflect tumour biology more directly than individual genomic alterations.

Methods: We conducted a narrative review of literature on mass spectrometry-based proteomics in PDAC, covering discovery and translational studies published up to 31 December 2025. PubMed and Scopus were searched using the terms 'PDAC proteomics', 'pancreatic cancer mass spectrometry', 'pancreatic cancer biomarkers', 'glycoproteomics', 'phosphoproteomics', 'extracellular vesicle proteomics' and related combinations. Studies were selected according to methodological relevance, sample type and translational context, encompassing tissue proteomics, plasma- and serum-based proteomics, secretome analysis, extracellular-vesicle proteomics, glycoproteomics, phosphoproteomics and spatially resolved proteomics. The THBS2/CA19-9 biomarker panel was used as a running case study to illustrate the translational arc from secretome-guided discovery to prediagnostic evaluation in independent cohorts.

Results: Tissue proteogenomics, led primarily by Clinical Proteomic Tumor Analysis Consortium initiatives, has defined protein-anchored molecular subtypes and signalling dependencies that cannot be predicted from genomic data alone, although translation into circulating biomarkers is constrained by secretion dynamics, plasma dilution and systemic background. Blood-based approaches remain technically demanding because of the extreme dynamic range of the plasma proteome. The THBS2/CA19-9 panel illustrates both the potential and the limitations of circulating strategies, showing strong diagnostic performance at clinical presentation but substantially attenuated sensitivity in prediagnostic samples. Secretome-guided discovery and EV proteomics provide biologically informed frameworks with growing translational potential, and recent multi-protein EV signatures incorporating ALPPL2 and THBS2 show promise for early detection. Glycoproteomic strategies targeting tumour-associated sialylation, fucosylation and truncated O-glycans offer biologically coherent routes to improving specificity beyond bulk CA19-9 quantification. Phosphoproteomics provides a direct readout of kinase-network activity, while mass spectrometry imaging, laser microdissection-coupled proteomics and complementary spatial platforms can help resolve the tumour–stroma admixture that confounds bulk analyses.

Conclusions: Proteomics provides functional and mechanistic insights into PDAC biology that are inaccessible through genomic or transcriptomic approaches alone. Translational progress requires precise alignment between biological compartment and clinical intent, rigorous validation in multiple independent cohorts under real-world confounding conditions, and integration of protein, glycan and nucleic-acid signals. Spatial proteomics and integrative multi-omics panels are particularly promising for resolving tumour–stroma heterogeneity and improving early detection in high-risk populations.

Keywords: Pancreatic ductal adenocarcinoma, PDAC; Proteomics, Mass spectrometry, Biomarkers, Glycoproteomics, Phosphoproteomics, Extracellular vesicles, Spatial proteomics, CA19-9, Liquid biopsy.

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1. Background

Pancreatic ductal adenocarcinoma (PDAC) remains one of the most lethal malignancies, with a median overall survival below one year in most clinical settings. This dismal prognosis reflects both its complex molecular architecture and the limited efficacy of current therapeutic strategies. Comprehensive genomic studies have shown that PDAC is shaped by recurrent alterations across key molecular pathways, including KRAS, TGF-β, WNT, NOTCH and ROBO/SLIT signalling, G1/S transition, SWI/SNF, chromatin modification, DNA repair and RNA processing, establishing a recurrent but heterogeneous molecular framework for the disease [1, 2]. These advances have refined molecular-subtype classification and clarified dominant oncogenic and differentiation-related programmes, underscoring the biological diversity of PDAC and its relevance to therapeutic development. Despite these advances, clinical translation has remained modest because tumour phenotypes are ultimately executed at the protein level. Translation, degradation, subcellular localisation and post-translational modifications (PTMs) determine the functional state of signalling networks. This is particularly relevant in PDAC, where desmoplastic remodelling, inflammatory signalling and therapeutic resistance are strongly mediated by extracellular-matrix (ECM) components, secreted factors and phosphorylation-dependent pathways. Proteomics can therefore complement genomic analyses by quantifying pathway activity, characterising stromal and immune contributions within the tumour microenvironment, and identifying circulating biomarkers that may more closely reflect functional tumour biology [3-6]. Contemporary proteomic research in PDAC incorporates several complementary analytical layers: global proteome profiling, phosphoproteomics, glycoproteomics and glycomics, secretome analysis, EV proteomics, and spatially resolved proteomics. This review examines each strategy in relation to its methodological basis, principal findings and realistic translational contribution.

2. Mass Spectrometry-Based Methods in PDAC Proteomics

As depicted in **Figure 1** and further detailed in Table 1 available in SM1, large-scale proteogenomic initiatives, most notably those conducted by the Clinical Proteomic Tumor Analysis Consortium (CPTAC), have demonstrated the value of integrating proteomic, phosphoproteomic and glycoproteomic data with genomic and transcriptomic profiles. These studies have refined molecular-subtype classification and revealed protein-level signalling features that are not fully captured by transcriptome-based analyses [7, 8]. A central analytical challenge in PDAC is its low neoplastic cellularity, together with substantial stromal and immune infiltration in bulk tumour specimens [9, 10]. This cellular heterogeneity profoundly influences protein quantification and downstream biological interpretation [9, 10]. Mass spectrometry (MS)-based proteomics supports biomarker discovery, molecular characterisation and analysis of tumour tissue, plasma, serum and EVs [11, 12]. Most discovery studies use high-resolution liquid chromatography–tandem mass spectrometry (LC–MS/MS) with label-free quantification (LFQ), either through data-dependent acquisition (DDA) or data-independent acquisition (DIA), including sequential window acquisition of all theoretical fragment ion spectra (SWATH-MS) workflows. Isobaric labelling strategies, such as tandem mass tags (TMT) and isobaric tags for relative and absolute quantitation (iTRAQ), provide an alternative route to multiplexed analysis [11, 12]. These workflows require careful experimental design, normalisation and control of batch effects. DIA is increasingly favoured in clinical proteomics because it improves quantitative completeness across large cohorts and is scalable to biobank-level studies [11, 12]. Comprehensive methodological reviews describe the implementation of these strategies across PDAC sample types [3, 11-13]. Although discovery proteomics frequently yields candidate biomarker signatures, successful clinical translation depends on stringent validation. Targeted proteomic approaches provide an established route from discovery to clinically deployable assays. These include selected reaction monitoring, also known as multiple reaction monitoring (SRM/MRM), on triple-quadrupole instruments and parallel reaction monitoring (PRM) on high-resolution platforms, usually supported by stable-isotope-labelled peptides and rigorous quality-control frameworks [14, 15]. Targeted MS is particularly relevant in PDAC because proposed biomarkers require validation in larger, independent and clinically heterogeneous cohorts, especially in the presence of confounding conditions such as pancreatitis and diabetes [16, 17]. Candidate discovery is rarely the principal bottleneck; robust validation under real-world clinical conditions ultimately determines translational success [16-18].

3. Tissue Proteomics and Proteogenomics

Tissue proteomics provides the most informative context for mechanistic discovery and therapeutic-target identification in PDAC. Proteogenomic studies have shown that proteomic layers refine tumour classification and identify signalling events that cannot be predicted from RNA expression alone. Large-scale CPTAC analyses revealed coordinated alterations in metabolic enzymes, ECM and stromal programmes, and phosphorylation-driven signalling networks, supporting the existence of protein-defined tumour subgroups with potential therapeutic implications [7]. Broader pan-cancer proteogenomic resources further confirmed that protein abundance and PTMs frequently diverge from transcriptomic patterns, underscoring the added value of direct proteomic measurement for pathway inference and target nomination [8]. More recent studies integrating tissue and serum proteomics continue to map PDAC phenotypes and nominate candidate biomarkers that overlap across compartments [13, 19]. The biological meaning of tissue-proteomic measurements is strongly dependent on sample composition. Bulk analyses of tumour tissue reflect a mixture of neoplastic, stromal, immune and normal pancreatic-cell proteins. Without accounting for neoplastic cellularity and cellular composition, proteins identified as putative tumour biomarkers may instead reflect stromal abundance rather than tumour-cell-intrinsic biology. Integrating proteomic measurements with genomic, transcriptomic and histopathological information can improve interpretation in the context of cellular heterogeneity [7-10]. Importantly, biological relevance in tumour tissue does not automatically translate into a clinically actionable

circulating biomarker. Secretion dynamics, vascular access, plasma dilution, proteolytic degradation and systemic background determine detectability in blood. Thus, mechanistic relevance in tissue does not necessarily confer analytical detectability or clinical utility in plasma or serum.

4. Blood-Based Proteomics: Plasma and Serum

Plasma- and serum-based proteomics offer clear advantages for early detection, risk stratification and longitudinal monitoring. However, the plasma proteome is one of the most analytically challenging biological matrices, exhibiting a dynamic range exceeding ten orders of magnitude and substantial inter-individual and pre-analytical variability [20, 21]. Contemporary workflows therefore require strict pre-analytical standardisation, including control of time to centrifugation, storage conditions, anticoagulant choice and freeze–thaw exposure [20, 22]. Abundant-protein depletion, enrichment and fractionation can improve proteome depth, but may introduce technical variability through sample loss and unintended co-depletion of low-abundance proteins bound to high-abundance carriers [20-23]. Large-scale LC–MS/MS workflows, including DIA-based pipelines, additionally require randomisation, quality control, normalisation, assessment and correction of batch effects where necessary, and orthogonal validation by targeted MS or immunoassays [14, 15, 20, 22]. Even under optimised conditions, performance observed at or shortly before clinical diagnosis frequently declines in prediagnostic samples, highlighting the importance of longitudinal cohort design and sampling of high-risk populations [17, 18]. The THBS2/CA19-9 biomarker panel illustrates this distinction. Initial studies reported strong diagnostic performance in symptomatic or newly diagnosed PDAC cohorts [16, 24].

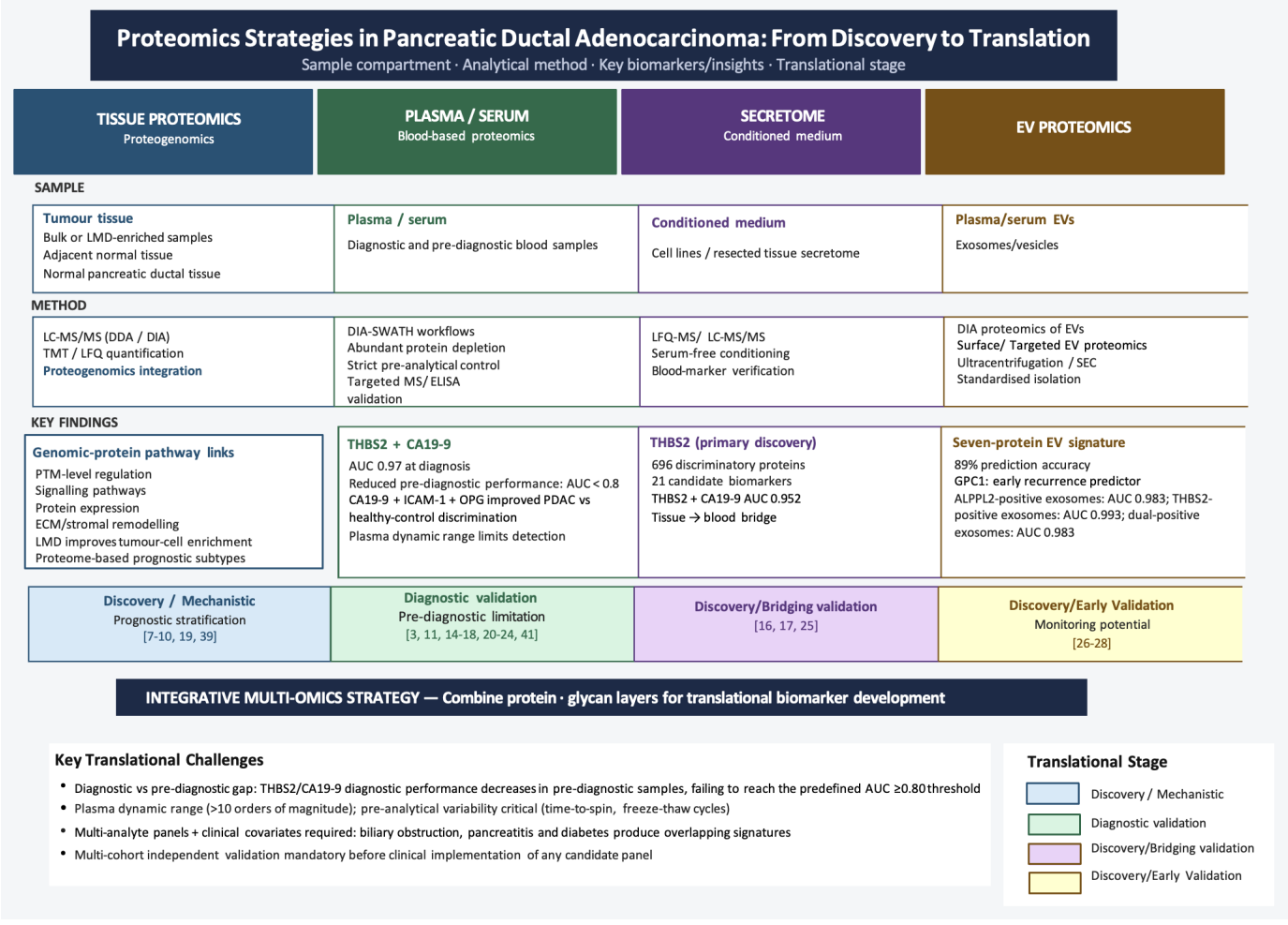

Figure 1a | Overview of proteomic and complementary analytical strategies in pancreatic ductal adenocarcinoma (PDAC), organised according to sample compartment, analytical method, key biomarkers or biological insights, and stage of translational development. Digital spatial profiling (DSP) and enzyme-linked immunosorbent assay (ELISA) are included as complementary non-mass spectrometry methods. Abbreviations: ALPPL2, alkaline phosphatase, placental-like 2; AUC, area under the curve; CA19-9, carbohydrate antigen 19-9; DDA, data-dependent acquisition; DIA, data-independent acquisition; ELISA, enzyme-linked immunosorbent assay; EV, extracellular vesicle; GPC1, glypican-1; ICAM-1, intercellular adhesion molecule 1; LC–MS/MS, liquid chromatography–tandem mass spectrometry; LFQ, label-free quantification; LMD, laser microdissection; MS, mass spectrometry; OPG, osteoprotegerin; PTM, post-translational modification; SWATH, sequential window acquisition of all theoretical fragment ion spectra; THBS2, thrombospondin-2; TMT, tandem mass tags.

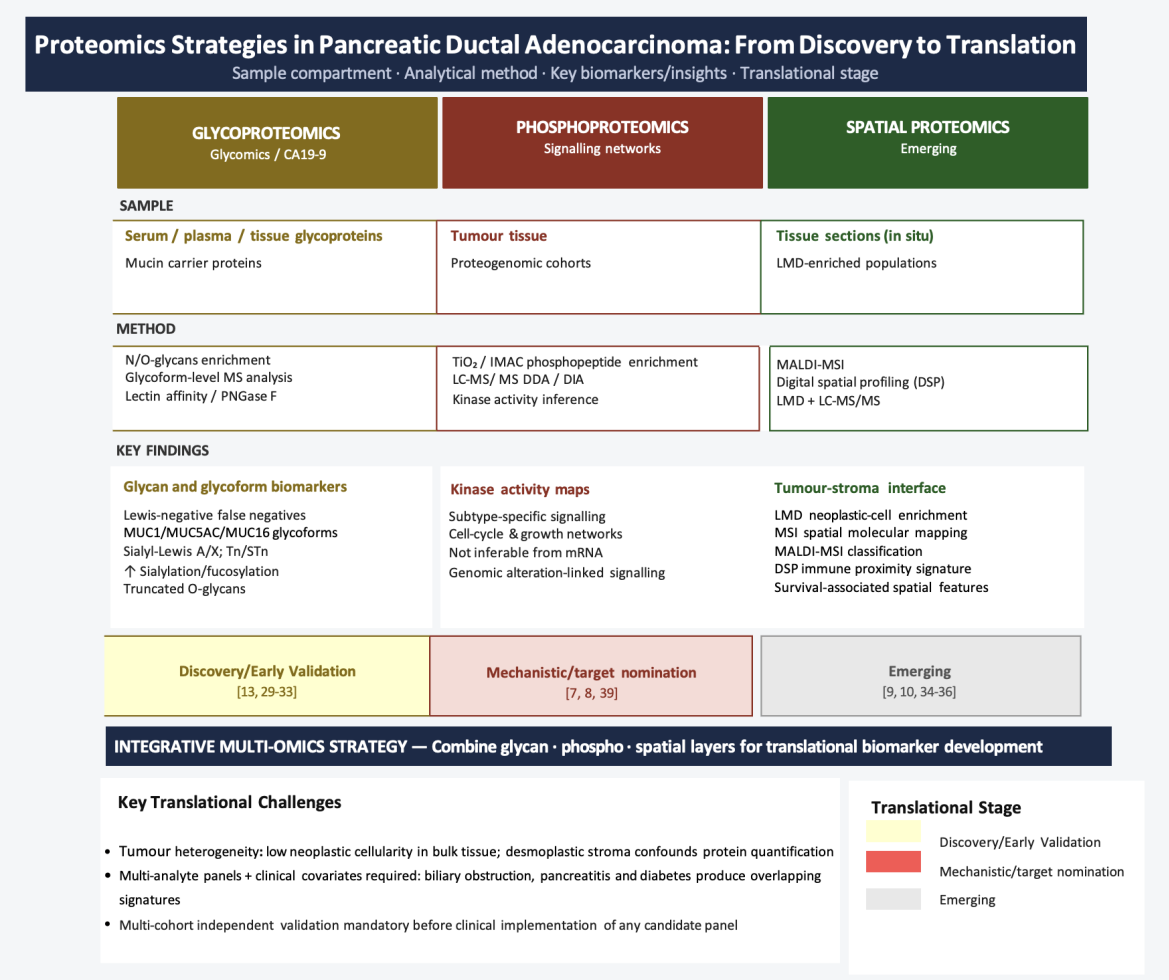

Figure 1b | Overview of proteomic and complementary analytical strategies in pancreatic ductal adenocarcinoma (PDAC), organised according to sample compartment, analytical method, key biomarkers or biological insights, and stage of translational development. Digital spatial profiling (DSP) and enzyme-linked immunosorbent assay (ELISA) are included as complementary non-mass spectrometry methods. Abbreviations: DDA, data-dependent acquisition; DIA, data-independent acquisition; DSP, digital spatial profiling; IMAC, immobilised metal affinity chromatography; LC–MS/MS, liquid chromatography–tandem mass spectrometry; LMD, laser microdissection; MALDI-MSI, matrix-assisted laser desorption/ionisation mass spectrometry imaging; MS, mass spectrometry; PNGase F, peptide-N-glycosidase F; SEC, size-exclusion chromatography.

However, performance was substantially reduced when the panel was evaluated in samples collected before diagnosis [18]. This discrepancy emphasises that early detection encompasses at least two distinct clinical problems: distinguishing PDAC from benign pancreatic disease at the time of diagnosis and detecting preclinical disease months before clinical manifestation. Study design must therefore align precisely with the intended clinical window [17, 18].

5. Secretome Proteomics

Secretome proteomics provides a rational bridge between tissue discovery and blood-based validation [25]. By profiling proteins actively secreted or shed by tumour cells and cells in the tumour microenvironment, this strategy enriches for candidates with a greater likelihood of being detectable in the circulation [25]. Thrombospondin-2 (THBS2) emerged through a secretome-oriented strategy and subsequently showed additive diagnostic value when combined with CA19-9 in plasma [16, 24]. The sequential workflow of secretome discovery, plasma verification and multi-cohort validation represents a biologically informed framework for improving translational plausibility in PDAC biomarker development [16, 24, 25].

6. Extracellular-Vesicle Proteomics

Extracellular vesicles, including small EV populations commonly described as exosomes, represent a promising liquid-biopsy compartment. EVs can concentrate tumour-derived proteins and protect molecular cargo from enzymatic degradation, potentially improving analytical sensitivity. Large-scale proteomic resources of circulating EVs are being developed to distinguish PDAC from benign pancreatic conditions and healthy controls [26]. Early enthusiasm surrounding individual EV-associated markers, particularly glypican-1-positive vesicles, stimulated rapid growth in the field. Subsequent studies, however, suggested that serum and exosomal glypican-1 may be more context-dependent and may relate to recurrence risk rather than providing a robust stand-alone diagnostic marker [27]. More recent studies have moved towards

multi-protein EV signatures incorporating markers such as ALPPL2 and THBS2, with greater emphasis on standardised isolation and analytical protocols [28]. Collectively, EV proteomics is converging on the broader principles of robust clinical proteomics: multi-analyte panels, rigorous controls and independent validation. The realistic contribution of proteomics to PDAC is therefore shaped by both sample type and clinical intent. Tissue proteomics provides direct insight into pathway activity, tumour–stroma interactions and therapeutic-target nomination; plasma and serum proteomics test whether candidate biomarkers remain detectable under stringent systemic constraints; secretome analysis increases the probability of identifying tumour- or stroma-derived proteins with properties compatible with detection in blood; and EV proteomics offers a tumour-enriched compartment with emerging translational potential. Much of the translational gap in PDAC proteomics stems not solely from analytical limitations, but also from inadequate alignment between biological compartment, analytical strategy and intended clinical use.

7. Glycoproteomics and Glycomics

PDAC is characterised by profound remodelling of the tumour glycome, including increased sialylation, enhanced fucosylation and expression of truncated O-glycans, particularly on mucins and other secreted glycoproteins. These changes are mechanistically linked to tumour progression, immune modulation and metastatic potential, reinforcing the biological relevance of glycomic and glycoproteomic approaches [29, 30]. CA19-9 (carbohydrate antigen 19-9) remains the most widely used serum biomarker in PDAC; however, it is a glycan epitope, sialyl-Lewis A, rather than a protein marker. This molecular identity underlies both its diagnostic value and its limitations. CA19-9 lacks specificity because concentrations may increase in benign conditions such as biliary obstruction and inflammatory pancreatic disease [3, 30]. Furthermore, Lewis-antigen-negative individuals cannot synthesise CA19-9, resulting in false-negative findings independent of tumour presence [31]. Total CA19-9 concentrations therefore reflect a composite signal influenced by tumour-associated glycosylation, inflammation and Lewis-antigen status. MS-based glycoproteomics can move beyond total CA19-9 quantification by enabling protein- and site-specific characterisation of glycoforms. These approaches may characterise glycan structures on defined carrier proteins, including mucins, and may potentially help distinguish tumour-associated glycosylation patterns from changes associated with benign inflammatory conditions [30, 32, 33]. This structural resolution allows interrogation of glycosylation changes that are biologically aligned with PDAC pathogenesis and may improve diagnostic specificity relative to measurements of total protein abundance alone. Reviews of the available evidence indicate that incorporating quantitative glycan characteristics or tumour-associated glycoforms may improve discrimination between PDAC and control or benign -disease groups in selected cohorts [30, 32, 33]. Nevertheless, large, multicentre validation studies, particularly in early-stage and prediagnostic populations, remain essential before clinical utility can be established. Overall, glycoproteomics represents one of the most biologically coherent strategies for the early detection of PDAC. By targeting tumour-associated glycosylation patterns, rather than relying exclusively on changes in total protein abundance that may also arise from inflammation, glycomic and glycoproteomic approaches interrogate a central biological axis in PDAC. [29, 30, 33].

8. Phosphoproteomics and Signalling-Network Analysis

Phosphoproteomics enables large-scale analysis of protein phosphorylation and provides a functional readout of intracellular signalling. In PDAC, this approach has been applied within proteogenomic frameworks to characterise oncogenic programmes and connect genomic alterations with downstream protein activity. Studies integrating genomic, transcriptomic, proteomic and phosphoproteomic layers have shown that phosphorylation data reveal kinase-network activity and pathway-activation states associated with molecular features of PDAC [7, 8]. These analyses connect mutations and molecular subtypes with downstream regulatory mechanisms, yielding functional insights that cannot be inferred from genomic data or protein abundance alone. Phosphoproteomic profiling has been particularly informative for nominating kinase-regulated vulnerabilities with potential therapeutic relevance, illustrating how PTM analysis adds functional resolution to PDAC biology [7, 8].

9. Spatially Resolved Proteomics

Spatially resolved proteomics is an emerging strategy designed to address the pronounced cellular heterogeneity and tumour–stroma admixture that characterise PDAC. Unlike bulk analyses, which yield averaged signals across mixed cell populations, spatial approaches localise protein expression to defined anatomical or cellular compartments. This capability is particularly relevant in PDAC, where neoplastic epithelium may constitute a minority of cells in a tumour specimen and the remaining signal is dominated by desmoplastic stroma, immune infiltrates and pancreatic parenchyma [9, 10]. Several complementary spatial technologies, including MS-based and antibody-based approaches, have been applied to PDAC. Mass spectrometry imaging, particularly matrix-assisted laser desorption/ionisation mass spectrometry imaging (MALDI-MSI), enables untargeted mapping of peptides and proteins directly from tissue sections at spatial resolutions ranging from tens to hundreds of micrometres [34, 35]. Multiplexed platforms such as DSP enable spatial comparison of tumour, stromal and immune protein expression in PDAC [36]. Laser microdissection followed by high-sensitivity LC–MS/MS provides a complementary MS-based route to deep proteomic profiling of physically isolated cell populations, generating genuinely compartment-specific measurements rather than computationally deconvolved estimates [9]. In PDAC, spatially resolved approaches are particularly relevant for characterising the tumour–stroma interface, quantifying protein gradients between desmoplastic stroma and neoplastic epithelium, and distinguishing tumour-cell-intrinsic alterations from signals driven by the abundant stromal compartment. These capabilities address one of the most persistent sources of interpretive error in bulk tissue proteomics. Although

spatial proteomics in PDAC remains less mature than spatial transcriptomics, its integration into multi-compartment workflows should refine mechanistic interpretation, biomarker specificity and identification of stromal therapeutic targets.

10. Proteomics in Precision Oncology

Proteomics is increasingly considered a complementary diagnostic layer within precision-oncology frameworks, particularly when genomic profiling does not reveal actionable alterations or fails to explain tumour behaviour fully. Because proteomic measurements capture protein abundance, pathway activity and post-translational regulation, they can provide functional information on signalling networks that is not apparent from DNA sequencing alone. Reviews addressing integration of proteomics into clinical decision-making highlight its potential role in molecular tumour boards, where multi-omics data are interpreted jointly to identify pathway-level vulnerabilities in individual patients [37]. Curated transcriptomic, proteogenomic and other open molecular resources also enable cross-study comparison and independent validation, both of which are critical to biomarker maturation. Open, well-annotated platforms allow investigators to compare findings across cohorts, harmonise analytical pipelines and evaluate candidates in independent datasets [38, 39]. Plasma proteome-wide and proteogenomic studies additionally seek to connect circulating protein concentrations with genetic-risk variants and molecular pathways involved in PDAC development, thereby identifying proteins that may serve as mechanistic biomarkers or therapeutic targets [40].

11. Limitations and Methodological Challenges

Several methodological and biological factors limit the robustness and reproducibility of proteomics-based biomarker studies in PDAC. Important variability arises during the pre-analytical phase. In plasma proteomics, the interval between blood collection and processing, storage temperature, repeated freeze–thaw cycles and haemolysis can alter protein composition and abundance, potentially obscuring biological differences between disease and control samples. Strict standardisation of sample handling is therefore essential to minimise technical artefacts [20-22]. Interpretation of tissue-proteomic data is further complicated by the complex cellular composition of PDAC tumours. Without accounting for neoplastic cellularity and cellular composition, proteins identified as putative tumour biomarkers may reflect stromal signals rather than neoplastic epithelial biology. Proteogenomic integration and spatially informed approaches can help address this problem, but they require matched multi-omic or compartment-resolved data that are not always available [7-10]. A persistent limitation of biomarker research is reliance on a single discovery cohort. Candidates that perform well in initial discovery cohorts frequently show reduced performance in independent validation cohorts, particularly when clinically relevant pancreatic and hepatobiliary control conditions, including chronic pancreatitis, biliary obstruction and diabetes, are included. These conditions produce overlapping molecular signatures that complicate discrimination between malignant and non-malignant states. Validation across multiple independent cohorts is therefore essential before a candidate can be considered clinically relevant [17, 18, 22]. An important distinction must also be maintained between diagnostic and prediagnostic performance. Many studies evaluate patients with clinically diagnosed PDAC and may therefore produce overly optimistic estimates of diagnostic accuracy. Biomarkers that perform well at diagnosis do not necessarily detect disease during asymptomatic stages relevant to screening. Longitudinal studies in high-risk or prediagnostic populations are critical for determining whether candidates can identify PDAC before clinical presentation [18]. Finally, individual biomarkers are unlikely to provide adequate sensitivity and specificity for PDAC detection given the biological heterogeneity of the disease. Multi-analyte panels that combine complementary molecular features have greater diagnostic potential. The THBS2/CA19-9 panel illustrates this principle, showing improved performance relative to either marker alone in diagnostic settings [16, 17]. Its reduced performance in prediagnostic samples nevertheless emphasises the need for longitudinal validation before biomarker panels can be translated into early-detection strategies [18].

12. Future Directions

Hybrid panels combining circulating proteins with cfDNA, including tumour-derived ctDNA, may improve early-stage PDAC discrimination [41]. Integration with glycosylation characteristics and clinical covariates such as age, bilirubin concentration and new -onset diabetes represents an additional direction that requires prospective validation [30]. Advances in EV-isolation methods and MS workflows, particularly DIA, are expected to improve the reproducibility and scalability of EV-based proteomic analyses [11, 26, 28]. Proteome-wide association studies that link circulating protein concentrations with genetic-risk variants represent another emerging direction for identifying mechanistic biomarkers and therapeutic targets [40]. A sustained focus on early-stage PDAC and precursor lesions remains a critical unmet need. Much of the current proteomic literature is based on clinically diagnosed or advanced tumours, potentially biasing biomarker discovery towards late-stage disease biology. Targeted studies of early lesions are required to identify molecular signatures that emerge during the earliest phases of tumour development [42]. Translation of proteomic biomarkers into clinical practice will probably require standardised targeted-MS assays validated through multicentre and interlaboratory studies. SRM/MRM and PRM allow specific and reproducible quantification of selected proteins, and the establishment of such assays represents a critical step towards clinical implementation of proteomics-based diagnostics in PDAC [14, 15].

13. Conclusions

MS-based proteomics has become a central platform for PDAC research, providing functional and mechanistic information that genomic and transcriptomic approaches cannot fully capture.

Across tissue, plasma, serum, secretome, EV, glycoproteomic, phosphoproteomic and spatial domains, proteomic strategies have expanded understanding of PDAC biology and generated a growing set of candidate biomarkers, although few have reached clinical implementation. The central lessons are consistent: translational success requires alignment between biological compartment and clinical intent; individual biomarkers are unlikely to capture the heterogeneous biology of PDAC; validation in multiple cohorts under clinically realistic confounding conditions is essential; and the distinction between diagnostic and prediagnostic performance must be addressed explicitly in study design. The THBS2/CA19-9 trajectory illustrates both the promise and the limitations of the current paradigm, with strong performance at diagnosis but attenuated performance in prediagnostic samples. Integrative multi-omics strategies, spatially resolved proteomics, and hybrid molecular panels combining protein, glycan and nucleic-acid signals are among the most promising directions. These approaches may help achieve reliable early detection in high-risk populations, the clinical setting in which proteomics could have its greatest impact in PDAC.

Competing interests

The authors declare that they have no competing interests.

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Authors contributions

R.A.P.F.C., J.L.C. and H.M.S. designed the review. R.A.P.F drafted the first version. J.L.C Supervised and corrected all subsequent versions done by R.A.P.F.C. and drafted the final one. H.M.S supervised and gave valuable suggestions to the final version. The authors declare that artificial intelligence-assisted tools were used solely for language editing and grammar checking during manuscript preparation. All scientific content, interpretation, and conclusions are the sole responsibility of the authors.

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