Int. J. Sci. R. Tech., 2025 2(8)
A Multidisciplinary peer-reviewed Journal
www.ijsrtjournal.com [ISSN: 2394-7063]

Original Article

Proteomics in Personalized Cancer Therapy: Advances, Applications, and Future Perspectives

Ishwari Jaiswal*, Ruturaj Kulkarni, Garima Singh, Vaishnavi Rindhe, Krutika Patil

Deogiri College Chhatrapati Sambhaji Nagar, Maharashtra, India

ABSTRACT

Proteomics is revolutionizing personalized cancer therapy by offering functional, real-time insights into tumor biology that genomics alone cannot fully capture. Cancer is a heterogeneous disease, exhibiting molecular diversity across patients and within individual tumors. Traditional treatment strategies often fail due to this complexity, resulting in resistance and relapse. Personalized oncology addresses this challenge by tailoring treatment to the unique molecular characteristics of a patient's tumor. Proteomics—the large-scale study of proteins—plays a pivotal role by directly analyzing the effectors of cellular function, including protein expression levels and post-translational modifications (PTMs) such as phosphorylation and ubiquitination. Advanced technologies like mass spectrometry, protein microarrays, and phosphoproteomics allow for precise quantification, biomarker discovery, and drug target validation. Proteomics enables identification of predictive and prognostic biomarkers, supports early cancer detection through liquid biopsy platforms, and helps stratify patients for targeted therapies based on their proteomic signatures. Furthermore, proteogenomic approaches integrating proteomic with genomic data offer a more comprehensive understanding of tumor biology, enhancing precision in diagnosis and treatment. Case studies across multiple cancer types—including breast, lung, ovarian, and prostate—demonstrate the clinical impact of proteomic insights. Despite challenges in data interpretation and standardization, the integration of bioinformatics, artificial intelligence, and high-throughput proteomic platforms is rapidly advancing clinical translation. This review highlights the indispensable role of proteomics in transforming cancer care, fulfilling the promises of precision oncology, and guiding the next generation of therapeutic interventions.

Keywords: Proteomics, Biomarkers, Mass Spectrometry, Post-translational Modifications, Precision Oncology, Cancer Diagnosis, Protein Profiling

INTRODUCTION

Cancer is a highly heterogeneous disease, characterized by genetic, epigenetic, transcriptomic, proteomic, and metabolic variability not only between patients but also within the same tumor microenvironment [1]. This heterogeneity significantly complicates the design of standardized therapies. Traditional treatment modalities such as chemotherapy, radiotherapy, and even some targeted therapies often fail to achieve complete remission due to this diversity, contributing to therapy resistance and disease recurrence. The challenge of intratumor and interpatient variability is compounded by clonal evolution, which further diversifies the tumor cell population during treatment [2]. Subpopulations of cancer cells with distinct molecular profiles may respond differently, leading to partial or ineffective therapeutic outcomes [3]. Thus, a shift from a "one-size-fits-all" approach to a more tailored strategy is urgently needed. Personalized or precision oncology addresses this variability by tailoring treatment strategies to the unique molecular characteristics of an individual's cancer. By utilizing omics technologies, including genomics, transcriptomics, and increasingly proteomics, it becomes possible to identify biomarkers that predict disease progression, drug response, and resistance [4]. In personalized cancer therapy, treatment decisions are based on the molecular signature of the tumor—such as mutations, protein expression levels, or post-translational modifications (PTMs)—rather than solely on histopathological classification. Clinical applications include selection of targeted drugs (e.g., EGFR

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

inhibitors in lung cancer), immunotherapies guided by PD-L1 expression, or treatment stratification using companion diagnostics [5]. While genomics has been instrumental in uncovering mutations and alterations associated with cancer, proteomics provides complementary and functionally relevant insights by directly measuring the proteins, which are the final effectors of cellular function [6]. Proteomic profiling serves several critical functions in oncology. It helps identify tumor-specific biomarkers, track dynamic changes in the proteome in response to therapy, and detect post-translational modifications such as phosphorylation and acetylation, which are crucial for regulating signaling cascades [7]. Additionally, proteomics enables the stratification of patients for targeted therapies based on their unique protein expression profiles. Recent advancements in mass spectrometry-based proteomics and protein microarrays have made it possible to analyze large sets of proteins from tumor biopsies, plasma, and other biofluids. These technologies facilitate the mapping of intracellular signaling networks, the discovery of resistance mechanisms, and the identification of actionable targets in real-time clinical settings [8]. Furthermore, integrative multi-omics approaches—particularly proteogenomics—combine genomic and proteomic data to provide a more comprehensive understanding of tumor biology. Initiatives like the Clinical Proteomic Tumor Analysis Consortium (CPTAC) have demonstrated how alterations in the proteome correlate with phenotypic heterogeneity and can influence treatment outcomes, reinforcing the role of proteomics in advancing precision medicine [9]. This review aims to provide a comprehensive overview of how proteomics is revolutionizing personalized cancer therapy. It begins by examining recent technological and analytical advancements in the field of cancer proteomics, shedding light on the innovations that are enhancing our ability to study proteins at scale and with greater specificity. The review then explores key clinical applications, including the discovery of biomarkers, the prediction of drug resistance, and the development of personalized therapeutic strategies tailored to individual patient profiles. In addition, it highlights the current challenges and outlines future directions for integrating proteomics into routine clinical oncology practice. By synthesizing the latest findings, this paper underscores the indispensable role of proteomics in fulfilling the promises of precision oncology and transforming cancer treatment paradigms. Figure No.1, illustrates how different sample types (tissue, serum, urine) feed into multi-omics analyses—including proteomics—to yield patient-specific insights that inform diagnostics, prognostics, and therapy selection

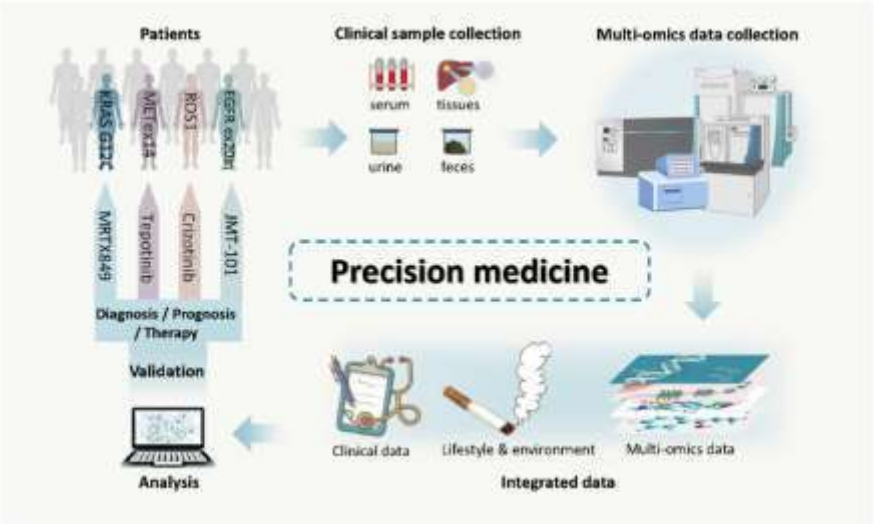

Figure No.1: Multi-omics pipeline for precision medicine

2. Basics of Proteomics

2.1 Definition and Scope

Proteomics is the large-scale study of proteins, encompassing their structure, function, modifications, and interactions within biological systems. Unlike the genome, which remains relatively stable, the proteome is highly dynamic and reflects the real-time

physiological and pathological conditions of cells [10]. In oncology, proteomics offers essential insights into the processes of tumorigenesis, metastasis, and drug resistance by profiling alterations in protein expression and post-translational modifications (PTMs) [11]. Within personalized medicine, the scope of proteomics is broad and impactful. It plays a key role in identifying cancer-specific biomarkers, uncovering distinct molecular subtypes of tumors, evaluating how individual patients respond to specific treatments, and monitoring disease progression as well as detecting minimal residual disease (MRD) [12]. By providing a detailed and functional understanding of the protein landscape, proteomics complements both genomics and transcriptomics, effectively bridging the gap between genetic information and phenotypic expression, and enhancing precision in cancer diagnosis and therapy.

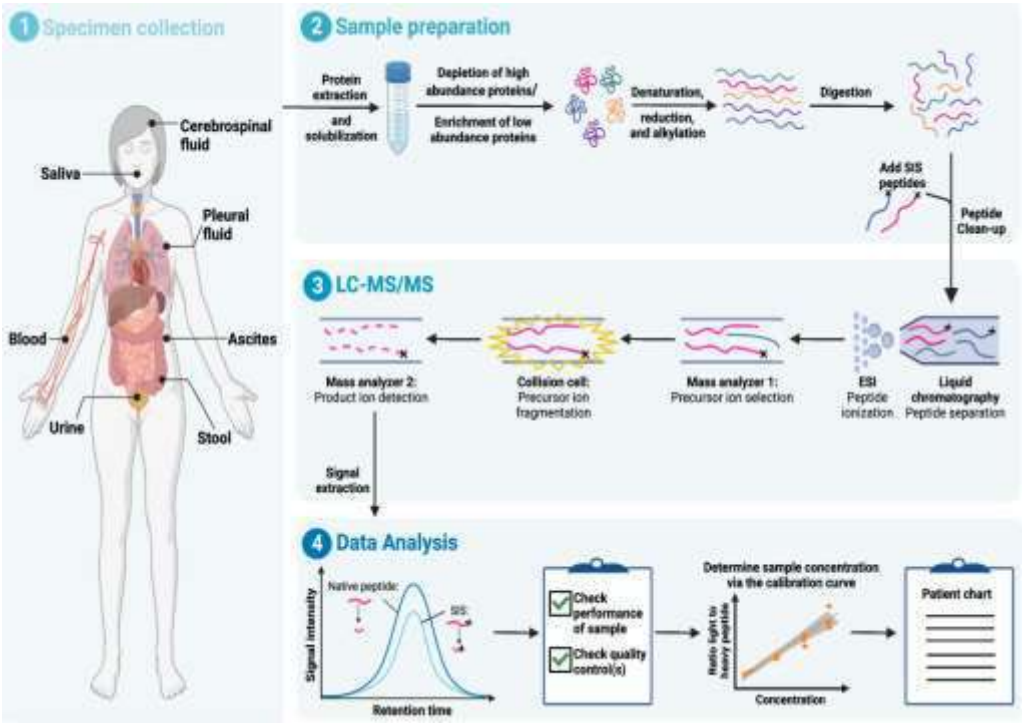

Figure No 2: Overview of a targeted proteomics workflow used in personalized cancer therapy.

The process begins with specimen collection from various biological fluids such as blood, urine, saliva, cerebrospinal fluid, and ascites. Sample preparation involves protein extraction, depletion of high-abundance proteins, enrichment of low-abundance proteins, denaturation, digestion, and peptide cleanup. Stable isotope-labeled standard (SIS) peptides are added to enable accurate quantification. The peptides are then analyzed using liquid chromatography-tandem mass spectrometry (LC-MS/MS), where precursor and product ions are selected and fragmented. Data analysis includes signal extraction, performance checking, and quantification through calibration curves, ultimately leading to clinical interpretation and decision-making in patient charts. This workflow highlights the critical role of proteomics in identifying clinically relevant biomarkers and informing individualized cancer treatment strategies.

2.2 Techniques in Proteomics

Proteomic analysis relies on several sophisticated technologies that enable the detection, quantification, and functional annotation of proteins in cancer tissues and fluids.

2.2.1 Mass Spectrometry (MS)

Mass spectrometry (MS) is the cornerstone of modern proteomics, providing high sensitivity and precision in the identification and quantification of proteins. This technique functions by ionizing peptides and measuring their mass-to-charge ratios, allowing for detailed analysis of complex protein mixtures. When combined with liquid chromatography (LC-MS/MS), mass spectrometry enables deep coverage of the proteome and supports a wide range of applications in cancer research. These include differential expression

analysis to compare protein levels across different conditions, mapping of post-translational modifications such as phosphorylation and ubiquitination, and integrating proteomic data with genomic information in cancer cohort studies [13]. Mass spectrometry has played a pivotal role in enabling landmark studies, such as those conducted by the Clinical Proteomic Tumor Analysis Consortium (CPTAC), which have led to the identification of actionable cancer subtypes in malignancies including breast, ovarian, and colorectal cancers [14]. This has significantly advanced the field of precision oncology by linking proteomic alterations to clinical outcomes and therapeutic strategies.

2.2.2 Two-Dimensional Gel Electrophoresis (2D-GE)

Two-dimensional gel electrophoresis (2D-GE) separates proteins based on their isoelectric point (pI) and molecular weight, and it was one of the earliest techniques developed in the field of proteomics. Despite the emergence of more advanced technologies, 2D-GE remains a valuable tool for several applications. It is particularly useful for visualizing protein isoforms, studying post-translational modifications (PTMs) and protein degradation products, and resolving thousands of proteins within a single sample [15]. However, the technique has notable limitations. Its reproducibility can be inconsistent, and it performs poorly when detecting hydrophobic or low-abundance proteins. These constraints have led to a decline in its routine use, especially as more sensitive and high-throughput methods have become available. Nonetheless, 2D-GE continues to play a role in specific proteomic analyses where its resolution capabilities are advantageous.

2.2.3 Protein Microarrays

Protein microarrays enable high-throughput screening of protein-protein interactions, antibody specificity, and protein expression levels, making them a powerful tool in proteomic research. There are two primary types of protein microarrays. Analytical arrays, such as antibody microarrays, are designed to detect specific proteins with high sensitivity and specificity. Functional arrays, on the other hand, are used to study protein interactions, post-translational modifications, and other functional aspects of proteins [16]. These microarrays are particularly valuable in oncology for applications such as biomarker validation and immune profiling. Their ability to simultaneously analyze thousands of proteins in a single experiment makes them an efficient and scalable platform for advancing personalized cancer diagnostics and therapeutic monitoring.

2.2.4 Label-Free and Labeled Quantification Methods

Quantification in proteomics can be achieved through both label-free and labeled methods, each offering distinct advantages depending on the experimental context. Label-free approaches involve comparing peptide intensities or spectral counts across multiple mass spectrometry runs. These methods are cost-effective and well-suited for analyzing large sample cohorts, making them ideal for population-scale studies. In contrast, labeled methods utilize isotopic or isobaric tags—such as iTRAQ, TMT, or SILAC—that enable the simultaneous analysis of multiple samples within a single mass spectrometry run [17]. These techniques provide greater accuracy and sensitivity, particularly for detecting subtle changes in protein expression levels. As a result, labeled approaches are often preferred in studies where precise quantification is critical, while label-free methods remain a practical choice for broad, exploratory proteomic analyses.

2.3 Bioinformatics in Proteomic Data Analysis

Proteomic datasets are inherently large, complex, and multi-dimensional, requiring sophisticated bioinformatics tools for meaningful interpretation. These tools play a vital role in various stages of data analysis. For instance, software such as Mascot and MaxQuant is used to identify peptides and proteins from mass spectrometry (MS) spectra. Functional enrichment analysis, using databases like Gene Ontology (GO) and KEGG, helps elucidate the biological significance of identified proteins. Integration of proteomic data with genomic and transcriptomic profiles—an approach known as proteogenomics—provides a more comprehensive view of cancer biology and enhances biomarker and target discovery [18]. Machine learning and network analysis techniques are increasingly employed to

predict therapeutic targets and stratify patients based on their molecular profiles. Visualization platforms such as Cytoscape are essential for mapping protein-protein interaction networks, enabling researchers to better understand signaling pathways and cellular mechanisms. Additionally, cloud-based platforms like cBioPortal, ProteomicsDB, and PRIDE Archive facilitate public access to annotated cancer proteomics datasets, supporting data sharing and collaborative research across the global scientific community [19].

3. Personalized Cancer Therapy: A Paradigm Shift

3.1 Concept and Evolution

Personalized cancer therapy—also referred to as precision oncology—marks a transformative shift in the way cancer is both understood and treated. Rather than relying on standardized treatment protocols for all patients with a particular type of cancer, this approach customizes interventions based on the unique molecular, genetic, and proteomic characteristics of an individual's tumor [20]. The foundation of this paradigm began with the sequencing of the human genome and was further advanced through large-scale initiatives like The Cancer Genome Atlas (TCGA). These efforts enabled the identification of oncogenic mutations, gene fusions, and copy number alterations across a wide range of cancers. As a result, targeted therapies were developed to address specific molecular alterations—for example, imatinib for BCR-ABL–positive chronic myeloid leukemia (CML), trastuzumab for HER2-positive breast cancer, and erlotinib for non-small cell lung cancer (NSCLC) harboring EGFR mutations [21]. However, despite these important genomic breakthroughs, it became evident that genetic alterations do not always correlate with protein expression levels or with a patient's actual response to therapy. This realization highlighted the critical need to integrate proteomic data into clinical decision-making, as proteomics offers a more direct and functional readout of cellular activity and treatment response.

3.2 Genomics vs. Proteomics in Personalization

While **genomics** provides a blueprint of potential cancer drivers, **proteomics** reveals the **functional state of the tumor**, offering dynamic insights into pathways that are actively involved in cancer progression and therapeutic resistance [22]. The table 1 is highlights the key differences between genomics and proteomics in terms of focus, temporal resolution, detection methods, clinical utility, and limitations.

Table 1: Comparative Analysis of Genomics and Proteomics in Cancer Research

Feature	Genomics	Proteomics
Focus	DNA/RNA mutations	Protein expression/modifications
Temporal resolution	Static (snapshot of potential)	Dynamic (real-time cellular state)
Detection methods	NGS, microarrays	MS, 2D-GE, protein microarrays
Clinical utility	Identifies potential targets, mutations	Reveals activated pathways, resistance mechanisms
Limitation	Does not reflect protein abundance or activity	High complexity, cost, and data interpretation

For instance, a mutation in **PIK3CA** may not result in pathway activation unless the downstream proteins are phosphorylated—something only proteomic profiling can determine [23]. Moreover, some therapeutic responses are governed not by DNA mutations but by **post-translational modifications** such as **phosphorylation, acetylation, or ubiquitination**—crucial aspects measurable by proteomics [24]. The integration of both omics has been demonstrated by studies like CPTAC, which combine proteogenomic approaches to better subtype tumors and stratify treatment [25].

3.3 Role of Biomarkers in Therapy Selection

Biomarkers are measurable indicators of biological processes or pharmacologic responses and play a critical role in personalized cancer therapy. Protein-based biomarkers, in particular, are essential for guiding various clinical decisions. They assist in

therapy selection, as seen with PD-L1 expression used to determine eligibility for immunotherapy. They also have predictive value; for instance, the expression of estrogen receptor (ER), progesterone receptor (PR), and HER2 informs the use of hormone therapy or anti-HER2 treatment in breast cancer. Additionally, protein biomarkers are used to monitor therapeutic response, such as prostate-specific antigen (PSA) levels in prostate cancer, and to detect emerging resistance, exemplified by the detection of the EGFR T790M mutation following resistance to first-generation EGFR inhibitors [26]. Proteomics has significantly advanced the discovery of both prognostic and predictive biomarkers through techniques like quantitative mass spectrometry profiling, reverse-phase protein arrays (RPPA), and artificial intelligence (AI)-driven biomarker panels [27]. For example, in patients with non-small cell lung cancer (NSCLC), plasma proteomics has been used to predict responses to PD-1/PD-L1 inhibitors by employing an immune-proteome–based scoring system known as I-SCORE [28]. Furthermore, the integration of artificial intelligence and machine learning has transformed biomarker interpretation. These technologies analyze vast and complex proteomic datasets to identify signature biomarker panels that are predictive of survival outcomes, treatment-related toxicity, and therapeutic efficacy, thereby enhancing the precision and effectiveness of personalized oncology care [29].

4. Proteomics in Cancer Diagnosis And Prognosis

4.1 Discovery of Novel Protein Biomarkers

The discovery of protein biomarkers plays a pivotal role in improving diagnostic accuracy and guiding therapeutic decision-making in oncology. Traditional diagnostic approaches, which often rely on histopathological grading and genetic testing, may fail to fully capture the functional abnormalities occurring within tumors. Proteomics has addressed this limitation through advanced technologies such as mass spectrometry and protein microarrays, which allow for the identification of cancer-specific proteins and post-translational modifications that more accurately reflect the tumor's real-time phenotype [30]. Proteomic profiling enables the detection of tumor-associated proteins in biological specimens such as serum, plasma, and tissue. These proteins can serve various clinical purposes: as diagnostic biomarkers—such as the overexpression of HER2 in breast cancer—as predictive biomarkers, exemplified by EGFR expression guiding the use of tyrosine kinase inhibitors, or as theranostic markers that inform both diagnosis and treatment strategies [31]. The development and application of cutting-edge proteomic tools, including iTRAQ, TMT, and label-free mass spectrometry platforms, have further accelerated the identification of low-abundance and functionally significant proteins across different cancer types [32]. These advancements continue to enhance the utility of proteomics in personalizing oncology care by providing more precise molecular insights into tumor biology.

4.2 Early Detection Through Proteomic Profiling

Early detection of cancer is one of the most effective strategies for improving patient survival, and proteomics plays a crucial role in achieving this goal. By enabling the detection of subtle changes in protein expression during the earliest stages of tumorigenesis—well before any morphological or radiological abnormalities are evident—proteomics provides a powerful tool for identifying cancer at its inception [33]. In ovarian cancer, for example, proteomic analyses have led to the discovery of serum proteins such as osteopontin and mesothelin, which demonstrate greater specificity than the commonly used biomarker CA-125 [34]. Similarly, in pancreatic cancer, plasma proteomic signatures involving galectin-3-binding protein and thrombospondin-1 (THBS1) have been associated with early-stage disease, offering a promising avenue for earlier intervention [35]. The integration of high-throughput proteomic techniques with machine learning algorithms has facilitated the development of multiplexed biomarker panels. These panels are capable of distinguishing between cancer subtypes with over 90% accuracy across several cancer types [36]. As a result, they are increasingly being incorporated into liquid biopsy platforms, enabling non-invasive early screening and enhancing the potential for timely and targeted treatment.

4.3 Prognostic Markers for Disease Progression

Prognostic biomarkers offer valuable insight into the likely course and aggressiveness of a disease,

independent of the specific treatment administered. Proteomic studies contribute significantly to this area by enabling the classification of tumors into molecular subtypes that are associated with distinct clinical outcomes. This stratification helps guide therapeutic decisions, particularly in determining the appropriate intensity of treatment based on the biological behavior of the tumor [37]. In the case of triple-negative breast cancer (TNBC), proteomic profiling has revealed the existence of distinct subgroups characterized by varying levels of immune activation and cellular proliferation, which correlate closely with patient prognosis [38]. Similarly, in non-small cell lung cancer (NSCLC), specific proteins such as KRT6A, SERPINA1, and SPP1 have been identified as markers linked to poor prognosis and an increased risk of metastasis [39]. Proteomic research has also highlighted the prognostic significance of the tumor microenvironment. For instance, in colorectal cancer, certain proteomic patterns reflecting stromal activation have been associated with a higher risk of recurrence. These findings underscore the importance of the surrounding tumor stroma in influencing disease progression and patient outcomes [40].

4.4 Case Studies: Breast Cancer, Lung Cancer, etc.

Breast Cancer

Breast cancer is one of the most extensively studied malignancies in the field of proteomics, leading to several important discoveries that have shaped clinical practice. A major milestone was the identification of HER2 overexpression, which became a key therapeutic target for the monoclonal antibody trastuzumab, significantly improving outcomes for HER2-positive patients. In addition to HER2, proteomic analyses have identified other proteins such as Annexin A1 and members of the S100 family, which are associated with more aggressive tumor phenotypes and poorer prognoses. Furthermore, proteomic subtyping has expanded the traditional classification of breast cancer beyond the established luminal and basal categories. These novel subgroups, defined by distinct protein expression patterns, have provided deeper insights into tumor biology and have proven useful in predicting treatment response, paving the way for more personalized therapeutic strategies [41].

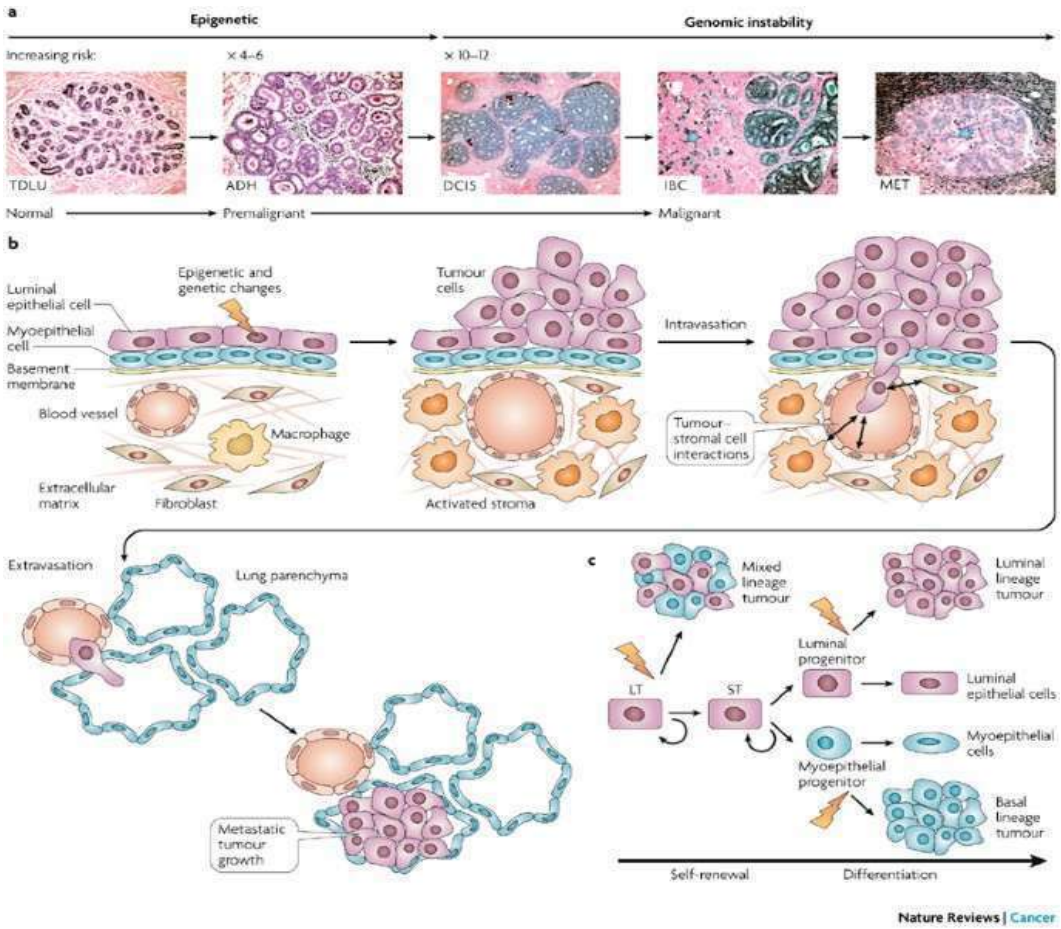

Figure No. 3. Progression, microenvironment, and lineage differentiation in breast cancer.

The figure No.1 illustrates the multistep progression of breast cancer from normal terminal ductal lobular units (TDLU) to metastatic disease (MET) through premalignant (ADH, DCIS) and malignant (IBC) stages (a). It also highlights the role of tumor–stromal interactions during invasion and metastasis (b), and the differentiation of breast tumors from distinct epithelial progenitor cell lineages, leading to luminal, basal, or mixed-lineage subtypes (c). These mechanisms underpin breast cancer heterogeneity and therapeutic response.

Lung Cancer

Proteomic advances have helped stratify **NSCLC** patients for immunotherapy. A notable example is the **I-SCORE** system, a plasma-based proteomic signature predictive of PD-1/PD-L1 inhibitor response [42]. Mass spectrometry has also uncovered markers such as *periostin*, *MMP9*, and *ENO1* in bronchoalveolar lavage fluid and plasma, contributing to early diagnosis and prognosis of lung cancer [43].

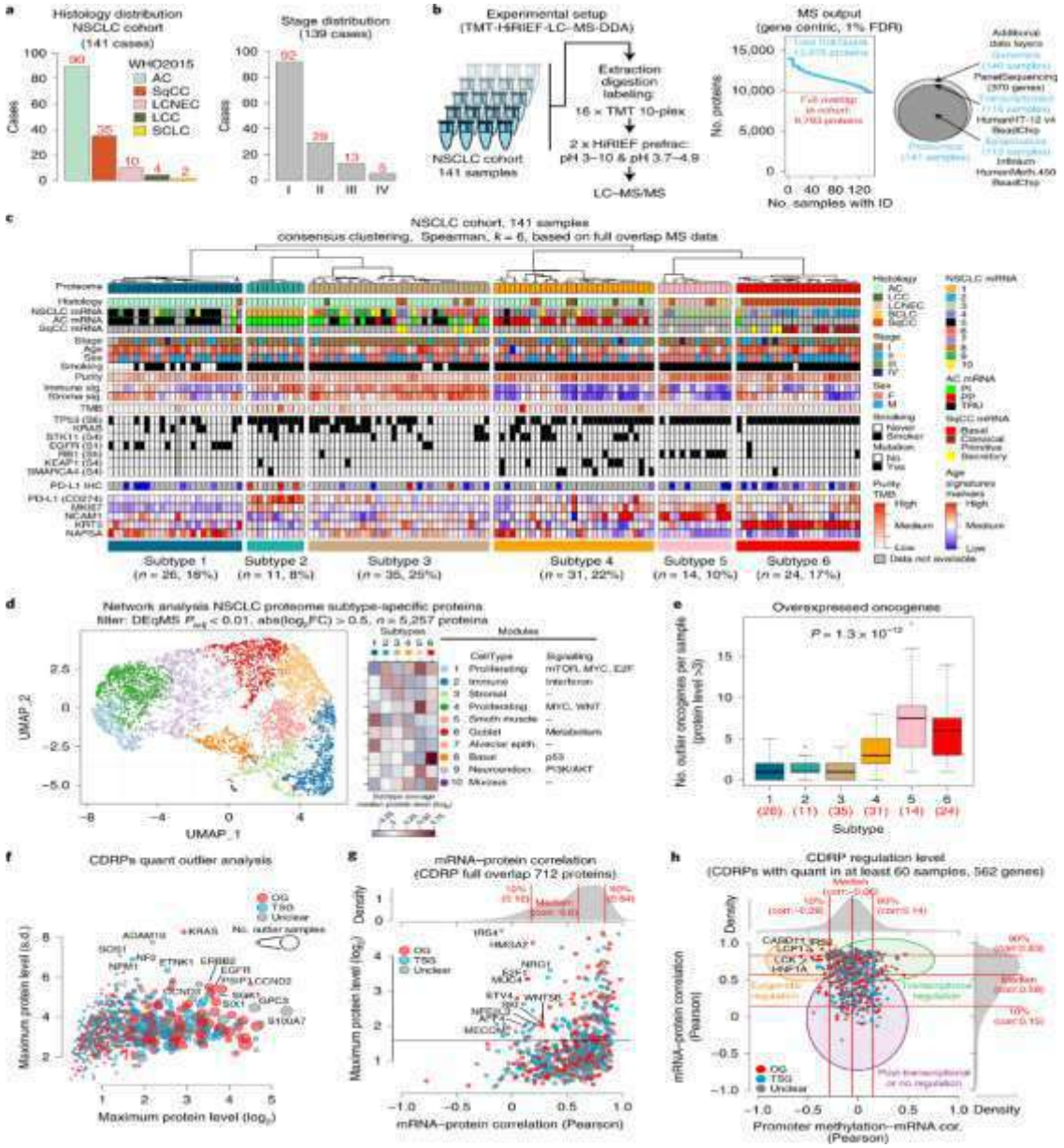

Figure No. 4. Proteomic stratification of NSCLC subtypes and their clinical, molecular, and immunological characteristics.

This figure No. 4, presents a large-scale proteomic analysis of 141 NSCLC tumor samples using TMT-based mass spectrometry. Consensus clustering based on protein expression identified six distinct molecular subtypes with varying histological, genomic, immune, and pathway features (a–c). Subtype-

specific proteins were further mapped via UMAP dimensionality reduction and network modules (d), showing differences in cell types and signaling pathways. Box plots show subtype-specific oncogene expression levels (e), while correlation plots (f–h) reveal quantitative discrepancies between mRNA and protein levels, influenced by transcriptional, post-transcriptional, and methylation regulation mechanisms.

Other Cancers

In ovarian cancer, proteomic profiling of high-grade serous ovarian carcinoma (HGSOC) has uncovered critical molecular pathways such as epithelial-mesenchymal transition (EMT) and the PI3K-Akt signaling cascade, both of which have emerged as potential targets for therapeutic intervention [44]. In prostate cancer, urinary proteomics has advanced risk stratification beyond the conventional prostate-specific antigen (PSA) test. Proteins such as alpha-methylacyl-CoA racemase (AMACR) and prostate cancer antigen 3 (PCA3) have been identified as more specific biomarkers, offering improved diagnostic accuracy and aiding in clinical decision-making [45].

5. Proteomic Approaches in Therapeutic Target Identification

5.1 Protein Expression and Post-Translational Modification Profiling

Therapeutic target discovery in oncology is increasingly reliant on proteomics to move beyond static genomic alterations and assess the actual functional molecules—proteins—that drive tumor behavior. By profiling protein expression, researchers gain valuable insights into which signaling pathways are active, which receptors are overexpressed, and how tumors dynamically adapt in response to therapy. Crucially, cancer progression is influenced not only by genetic mutations but also by post-translational modifications (PTMs), which significantly affect protein function and cellular behavior. These modifications include phosphorylation, which plays a central role in intracellular signaling cascades; ubiquitination, which regulates protein stability and degradation; acetylation and methylation, which are involved in epigenetic control; and glycosylation, which can modulate immune evasion and cell adhesion mechanisms [46]. Mass spectrometry-based phosphoproteomics has become a powerful tool for mapping phosphorylation events within tumors, enabling the identification of druggable kinases such as AKT, mTOR, and EGFR. The work of the Clinical Proteomic Tumor Analysis Consortium (CPTAC) has shown that PTM-based proteomic profiling provides both predictive and prognostic information that often surpasses what genomic data alone can offer [47]. A notable example of this is the identification of hyperphosphorylation of HER2 and CDK1 as markers of aggressive breast cancer phenotypes, which are particularly responsive to targeted kinase inhibitors [48]. This highlights the growing importance of proteomics in guiding the development of precision therapies in cancer treatment.

5.2 Drug Target Validation Using Proteomic Technologies

Once potential therapeutic targets are identified, validation is a critical step to confirm their clinical relevance and functional significance. Proteomics provides a range of powerful tools that not only confirm target engagement but also help elucidate the mechanism of action (MoA) of candidate drugs.One widely used method is Thermal Proteome Profiling (TPP), which detects direct drug-protein interactions by measuring changes in protein thermal stability within living cells. This approach helps identify whether a drug binds specifically to its intended target or affects other proteins, revealing potential off-target effects [49]. Another technique, chemical proteomics, employs activity-based probes or affinity tags to isolate and identify interacting proteins, thereby determining binding specificity and functional interactions at a molecular level [50]. Additionally, Reverse Phase Protein Arrays (RPPA) are used to validate target protein expression and activation status across large sample cohorts, often with the aid of phosphorylation-specific antibodies [51]. An illustrative example of TPP's utility is its application in acute myeloid leukemia, where it confirmed BRD4 as a direct target of BET inhibitors. Moreover, the method also uncovered off-target effects that could contribute to drug toxicity or therapeutic resistance [52]. These proteomic strategies collectively ensure that potential targets are not only mechanistically understood but also clinically actionable, advancing

the translation of proteomic discoveries into effective cancer therapies.

5.3 Examples of Identified Targets in Various Cancers

Proteomics-driven target discovery has significantly advanced therapeutic strategies across a range of cancers, enabling the development of novel treatments and the repurposing of existing drugs based on functional protein data.In breast cancer, proteomic techniques such as reverse-phase protein arrays (RPPA) and phosphoproteomics have revealed both overexpression and hyperphosphorylation of HER2, directly informing the use of HER2-targeted therapies [53]. Additionally, activation profiles of cyclin-dependent kinases CDK4/6 have been associated with resistance to endocrine therapy, prompting the clinical adoption of CDK inhibitors as a complementary strategy [54]. Lung cancer research, particularly in non-small cell lung cancer (NSCLC), has also benefited from proteomic insights. Proteomic screening identified the expression of ALK fusion proteins in certain NSCLC subtypes, which led to the targeted use of crizotinib. Furthermore, plasma proteomics has uncovered proteins such as ENPP1 and periostin as predictive biomarkers of response to immune checkpoint inhibitors (ICIs), helping refine immunotherapy strategies [55]. In colorectal cancer, proteomic analyses have shown hyperactivation of the EGFR and PI3K-AKT pathways in RAS wild-type tumors, suggesting a potential benefit from dual-targeting therapies. In addition, proteomics has highlighted the role of stromal components, identifying fibronectin and tenascin-C within the tumor microenvironment as potential therapeutic candidates [56]. Ovarian cancer, particularly high-grade serous ovarian carcinoma (HGSOC), has also been a focus of proteomics and phosphoproteomics studies, which have identified SRC-family kinases and the mTOR pathway as key therapeutic vulnerabilities. These findings open up opportunities for targeted intervention in an otherwise challenging cancer type [57]. In prostate cancer, urinary proteomics has led to the identification of alpha-methylacyl-CoA racemase (AMACR), a protein that serves as both a diagnostic and therapeutic biomarker, providing a non-invasive tool for stratification and intervention [58]. Collectively, these examples underscore the power of proteomics not only to identify overexpressed proteins but also to provide functional context. This enhances the precision of drug development pipelines and supports the design of more effective combination therapies tailored to the specific molecular landscape of each cancer type.

6. Proteomics in Drug Resistance And Sensitivity

6.1 Mechanisms of Resistance Revealed by Proteomics

One of the major challenges in cancer therapy is the development of drug resistance, which often leads to treatment failure and disease relapse. While genomic analyses can identify resistance-associated mutations, it is proteomics that offers a deeper understanding of the functional changes at the protein level that drive adaptive resistance mechanisms. Proteomic investigations have revealed several critical pathways and processes involved in resistance. One such mechanism is the activation of alternative or bypass signaling pathways; for instance, in lung cancer, activation of MET or IGF1R has been observed following inhibition of EGFR, enabling the tumor to circumvent the therapeutic blockade. Another mechanism involves post-translational modifications, such as phosphorylation events on downstream effectors, which can restore signaling activity despite receptor inhibition. In addition, proteomics has uncovered resistance mechanisms linked to epigenetic reprogramming and the expression of protein isoforms—changes that are often missed by transcriptomic analyses [59]. A concrete example comes from phosphoproteomic studies of non-small cell lung cancer (NSCLC), where resistance to EGFR inhibitors was found to be driven by compensatory signaling through SRC and AXL kinases. These kinases bypass the EGFR blockade and sustain proliferative signals [60]. Similarly, in breast cancer, mass spectrometry-based profiling showed that resistance to trastuzumab was associated with increased phosphorylation of HER3 and reactivation of the PI3K pathway, both of which undermine the effectiveness of HER2-targeted therapy [61]. Proteomic studies have also highlighted the role of the tumor microenvironment in mediating drug resistance. Proteins such as cytokines and components of the extracellular matrix have been shown to affect drug uptake and promote immune evasion, further complicating therapeutic outcomes [62]. These

insights emphasize the importance of proteomics in uncovering complex, dynamic resistance mechanisms and guiding the development of more effective, adaptive cancer treatment strategies.

6.2 Predictive Proteomic Markers for Chemotherapy Response

Predicting individual patient responses to chemotherapy remains a significant clinical challenge, but proteomic technologies are emerging as powerful tools to address this issue. By identifying predictive biomarkers associated with drug sensitivity or resistance, proteomics enables more precise patient stratification and personalized treatment planning. Several studies have demonstrated the utility of proteomic profiling in uncovering protein markers linked to specific chemotherapy responses. For instance, elevated expression of ERCC1 has been associated with resistance to platinum-based chemotherapy in both lung and ovarian cancers, while high levels of TOP2A have been linked to a better response to anthracyclines in breast cancer. Similarly, the presence of glutathione S-transferase P1 (GSTP1) has been correlated with resistance to alkylating agents in colon cancer, indicating that protein expression can serve as a valuable predictor of treatment efficacy [63]. In colorectal cancer, quantitative proteomic analysis has identified thymidylate synthase (TS) and dihydropyrimidine dehydrogenase (DPD) as strong predictors of response to 5-fluorouracil (5-FU)–based chemotherapy regimens [64]. Likewise, in ovarian cancer, high expression levels of heat shock protein 90 (HSP90) have been linked to poor response to cisplatin, suggesting potential avenues for treatment optimization based on proteomic markers [65]. Beyond individual biomarkers, advanced machine learning techniques are now being integrated with proteomic datasets to enhance predictive accuracy. Approaches such as SHAP (SHapley Additive exPlanations)-based biomarker interpretation are being used to generate clinically relevant predictive signatures, enabling oncologists to anticipate therapeutic outcomes with greater confidence and tailor treatments accordingly [66].

6.3 Proteomic-Guided Therapy Adjustment

Proteomic profiling serves not only to guide the initial selection of cancer therapies but also to facilitate real-time adaptation of treatment strategies by monitoring changes in protein expression and signaling dynamics throughout the course of therapy. This dynamic capability allows clinicians to make timely therapeutic adjustments in response to molecular shifts observed during treatment. One notable application involves modifying kinase inhibitor regimens based on evolving phosphoproteomic landscapes. For example, in non-small cell lung cancer (NSCLC) patients who develop resistance to EGFR inhibitors, proteomic analyses have revealed ALK upregulation, prompting a switch to ALK-targeted therapies. Similarly, the integration of immune-proteomic data has proven valuable in assessing eligibility for immune checkpoint inhibitors (ICIs) and in fine-tuning dosage to improve therapeutic response while reducing adverse effects. Additionally, the monitoring of minimal residual disease (MRD) through liquid biopsies has been enhanced by detecting circulating tumor-derived proteins in plasma or urine, offering a non-invasive means of tracking tumor dynamics [67]. In clinical practice, dynamic proteomic assays such as longitudinal plasma proteomics and treatment response proteomics (TRP) are increasingly being used to predict early relapse, assess tumor adaptation to therapy, and identify emerging mechanisms of resistance [68]. These proteomic strategies have shown significant promise in cancers such as pancreatic, lung, and melanoma, where they help refine treatment plans in a personalized manner. By continuously evaluating the tumor's molecular profile, clinicians can maximize the therapeutic window—delivering the most effective treatment while minimizing unnecessary toxicity and improving overall patient outcomes.

7. Clinical Applications and Trials

7.1 Proteomics-Based Diagnostics in Clinical Practice

The integration of proteomics into clinical oncology is redefining how cancer is diagnosed and treated by offering real-time insights into the molecular behavior of tumors. Proteomics-based diagnostic tools are already being utilized or are approaching clinical implementation, providing valuable capabilities in

cancer subtype classification, drug-response prediction, minimal residual disease (MRD) monitoring, and treatment stratification. Techniques such as mass spectrometry (MS), reverse-phase protein arrays (RPPA), and immunoassays are employed to measure protein expression in clinical specimens, including plasma, tumor biopsies, and urine. These tools have been effectively applied in a range of cancers. For instance, in breast cancer, proteomic assays are used to assess HER2 expression; in prostate cancer, proteins such as PCA3 and TMPRSS2 fusion products are used for diagnosis; and in lung cancer, PD-L1 levels are quantified through immunohistochemistry and MS-based approaches to guide immunotherapy decisions [69]. Furthermore, artificial intelligence–driven proteomic platforms have emerged as powerful aids for clinicians, offering data interpretation through decision-support systems. Classifiers trained on proteomic data can distinguish between patients likely to respond to specific treatments, such as immunotherapies, and those who are not, thereby enhancing the precision and personalization of cancer care [70].

7.2 Current Clinical Trials Using Proteomic Strategies

An increasing number of clinical trials are incorporating proteomic profiling to enhance patient stratification, guide treatment decisions, and validate biomarkers. These trials span a broad spectrum, from early-phase studies focused on biomarker discovery to advanced-phase trials evaluating therapeutic efficacy. One ongoing example is clinical trial NCT04335006, which is examining plasma proteomic signatures in patients with metastatic non-small cell lung cancer (NSCLC) undergoing treatment with immune checkpoint inhibitors. Similarly, trials linked to the Clinical Proteomic Tumor Analysis Consortium (CPTAC) are bridging the gap between research and clinical application by correlating genomic and proteomic alterations with treatment responses in ovarian, breast, and colorectal cancers [71]. Another notable trial, NCT03895684, is evaluating the predictive potential of urine proteomics in determining response to androgen deprivation therapy in prostate cancer. Additionally, the APOLLO network (Applied Proteogenomics Organizational Learning and Outcomes), part of the NCI-MATCH trial extension, is a nationwide U.S. initiative aimed at integrating proteomic data into routine oncology practice [72]. These clinical studies employ a range of advanced proteomic platforms. Liquid chromatography-tandem mass spectrometry (LC-MS/MS) is used for global proteomic profiling, while methods such as SWATH-MS and data-independent acquisition (DIA-MS) provide reproducible, clinical-grade data. For quantitative biomarker validation, targeted proteomics techniques like multiple reaction monitoring (MRM) and selected reaction monitoring (SRM) are applied, supporting robust and scalable clinical translation.

7.3 FDA-Approved Proteomic Biomarkers and Companion Diagnostics

Although **genomic biomarkers** dominate FDA approvals, **proteomic biomarkers** have also gained ground—particularly in areas like early detection, treatment monitoring, and immunotherapy response. Some **notable FDA-approved proteomic-based diagnostics** and **companion diagnostics** include:

Biomarker	Indication	Technology	Approval
HER2	Breast/gastric cancer	IHC/FISH & proteomic scoring	Trastuzumab companion Dx [73]
PD-L1	NSCLC, urothelial cancer	IHC & MS-based quantitation	Pembrolizumab, Atezolizumab
PCA3	Prostate cancer risk stratification	Urinary protein assay	Diagnostic aid
OVAL Protein Signature	Ovarian cancer detection	MS-based plasma panel	FDA Breakthrough Device (2022) [74]

Additionally, the **MSK-IMPACT** and **Foundation One CDx** platforms are beginning to include **proteogenomic features**, foreshadowing a broader FDA landscape for integrated proteomic diagnostics.

8. Challenges and Limitations

Despite its transformative potential, clinical proteomics in personalized cancer therapy faces several **technological, computational, and regulatory hurdles** that hinder full-scale implementation. These challenges must be systematically addressed to ensure consistent translation from discovery to bedside.

8.1 Technical Limitations in Sample Handling and Analysis

Pre-analytical variability—including factors such as sample collection, storage, and processing—remains one of the primary bottlenecks in proteomic studies. Unlike DNA, proteins are inherently more fragile and are highly sensitive to environmental conditions such as temperature, enzymatic degradation, and pH fluctuations. Additionally, proteins can be significantly affected by freeze–thaw cycles and delays in processing time, all of which can compromise sample integrity. The quality of biological samples has a direct impact on downstream analyses, especially in mass spectrometry (MS), where even minor handling errors can result in the loss or alteration of low-abundance proteins, thereby skewing results [75]. A further complication arises from the vast dynamic range of protein concentrations in biological fluids such as plasma or serum, which can span up to ten orders of magnitude. This wide range presents a substantial challenge for detecting low-abundance biomarkers, as highly abundant proteins can mask their presence or interfere with accurate quantification [76]. Together, these issues highlight the critical need for stringent sample handling protocols and advanced analytical methods to improve the reliability and reproducibility of proteomic data.

8.2 Data Complexity and Reproducibility

Proteomic datasets are inherently large, multidimensional, and heterogeneous, necessitating substantial computational infrastructure and specialized expertise for analysis and interpretation. One of the primary challenges lies in the significant inter-laboratory variability that arises from differences in sample preparation protocols, instrument calibration procedures, and peak calling methods. This variability often complicates data comparability and integration across studies. Additionally, inconsistencies in protein annotations between major databases such as UniProt and Ensembl can lead to discrepancies in protein identification and functional interpretation, further complicating data analysis [77]. Another major issue is the limited reproducibility of proteomic findings across independent cohorts, often due to batch effects or the use of different mass spectrometry (MS) platforms. In contrast to the field of genomics, where next-generation sequencing (NGS) workflows have become largely standardized, proteomics still lacks universally accepted analytical pipelines—particularly for specialized tasks like post-translational modification (PTM) profiling and label-free quantification [78]. Furthermore, the process of peptide identification is susceptible to high false discovery rates (FDR), especially when analyzing modified peptides or novel isoforms. This not only reduces confidence in individual findings but also adds a significant layer of complexity to data interpretation, underscoring the need for more rigorous validation and standardized computational frameworks in clinical proteomics.

8.3 Standardization and Regulatory Issues

The clinical adoption of proteomics continues to face significant obstacles due to the absence of standardized protocols and well-defined regulatory frameworks. Regulatory agencies such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have yet to establish comprehensive validation criteria for proteomic-based diagnostic tests, making the process of gaining clinical approval both complex and time-consuming. One of the key challenges is the lack of assay harmonization across different laboratories and analytical platforms, which leads to inconsistencies in data quality and reproducibility. Furthermore, there is a notable absence of certified reference materials that are essential for quantitative proteomics, making it difficult to benchmark results or ensure accuracy across studies. Another critical concern is the absence of clear validation criteria for multiplex assays, especially those that integrate proteomic data with artificial intelligence (AI) algorithms [79]. The increasing complexity of diagnostic platforms—often involving multi-marker panels combined with

machine learning—raises important questions about their clinical utility, interpretability, and reproducibility. In addition, the evolving nature of AI-supported diagnostics introduces concerns regarding regulatory oversight and potential liability. Until these scientific, technical, and regulatory issues are adequately addressed, the widespread clinical implementation of proteomics will remain limited [80].

8.4 Integration with Other Omics Data

While proteomics offers valuable functional insights into cancer biology, it must be integrated with genomics, transcriptomics, and metabolomics to provide a comprehensive molecular portrait of the disease. However, this multi-omics integration faces several significant challenges. One major hurdle is the difference in data scales and formats, such as continuous measurements in some datasets versus categorical data in others, which complicates their combined analysis. Additionally, there is a lack of standardized analytical frameworks designed to effectively merge diverse omics data types. The computational demands of joint modeling are substantial, requiring advanced artificial intelligence tools and significant processing power to manage and interpret the complex datasets. Proteogenomics, an integrative approach championed by initiatives like the Clinical Proteomic Tumor Analysis Consortium (CPTAC) and the APOLLO network, has demonstrated considerable success in identifying novel therapeutic targets and refining disease classification. Despite these achievements, such integrative methods depend heavily on the availability of high-quality, matched multi-omic samples, as well as robust cross-platform normalization strategies to ensure data comparability. Moreover, collaborative networks and shared data repositories are essential to facilitate data sharing and joint analyses across research groups [81]. Without reliable frameworks for integration, critical biological insights risk remaining siloed within individual omics layers, thereby limiting the full potential of precision oncology to deliver personalized and effective cancer treatments.

FUTURE PERSPECTIVES

Proteomics is poised to play a transformative role in the next era of personalized cancer therapy. The future of this field will be characterized by deeper integration with multi-omics platforms, more spatial and temporal resolution through single-cell and real-time technologies, and expanded roles in immunotherapy and cancer vaccines. These advancements promise to reshape clinical decision-making by offering dynamic, patient-specific insights into tumor biology.

9.1 Integration with Genomics, Metabolomics, and AI

While genomics and transcriptomics provide the foundational blueprint of disease, proteomics captures its functional execution by revealing protein abundance, modifications, and activity. The future of precision oncology will increasingly rely on the integration of multiple omics layers to construct comprehensive, systems-level models of cancer biology. Genomics plays a crucial role in identifying mutations, whereas proteomics sheds light on activated signaling pathways and potential therapeutic targets. Complementing these, metabolomics offers valuable insights by profiling metabolic alterations driven by enzymatic activities, thereby adding another dimension to the molecular characterization of tumors. Artificial intelligence (AI) and machine learning are indispensable tools for processing and interpreting the vast, heterogeneous datasets generated across these diverse omics platforms. Initiatives like the Clinical Proteomic Tumor Analysis Consortium (CPTAC) have already demonstrated the power of combining proteomic and genomic data to uncover clinically actionable cancer subtypes, underscoring the value of multi-omics integration [82, 83]. Looking ahead, key future directions include the development of multi-modal decision-support systems powered by AI, which can integrate complex omics data to guide clinical decision-making. Predictive models leveraging integrated omics signatures hold promise for forecasting treatment responses more accurately. Additionally, the creation of digital twins—computational simulations of tumor evolution and therapeutic outcomes—offers a transformative approach to personalize and optimize cancer treatment strategies [84].

9.2 Single-Cell Proteomics

Traditional proteomics typically analyzes bulk tissue samples, which can obscure the important intra-tumoral heterogeneity that plays a critical role in therapy resistance. Single-cell proteomics (SCP) addresses this limitation by enabling the characterization of protein expression at the individual cell level, thus providing a more detailed understanding of tumor complexity. Emerging SCP technologies include methods such as Single-Cell ProtEomics by Mass Spectrometry (SCoPE-MS), mass cytometry (CyTOF), and microfluidic immunoassays designed for ultra-low input quantification [85]. These advanced techniques allow researchers to investigate previously inaccessible cellular details. In cancer research, SCP has been applied to identify rare resistant cell clones and mechanisms of immune evasion, map cellular differentiation pathways involved in tumor progression, and uncover distinct phenotypes of tumor-infiltrating immune cells that predict responses to immune checkpoint inhibitors (ICIs) [86]. As the sensitivity and throughput of SCP technologies continue to improve, this approach is expected to become a fundamental tool in personalized cancer therapy, especially for solid tumors and hematologic malignancies where cellular diversity is particularly pronounced.

9.3 Real-Time Proteomic Monitoring

Real-time or longitudinal proteomics allows for the dynamic monitoring of tumor behavior throughout the course of therapy, moving beyond static snapshots to capture adaptive resistance, drug response, and minimal residual disease (MRD) in a time-resolved manner. This approach leverages several advanced techniques, including liquid biopsy-based proteomics from sources such as blood, saliva, and urine, microfluidic-integrated biosensors, and emerging wearable diagnostic devices currently under development [87]. Clinically, real-time proteomics offers significant benefits, such as the early prediction of treatment failure before it becomes apparent on imaging, the molecular-level detection of tumor relapse, and the continuous personalization of treatment regimens tailored to the evolving tumor profile. Platforms like Treatment Response Proteomics (TRP) and P-Monitor are currently being piloted in various cancer centers to assess the feasibility and effectiveness of bedside proteomic surveillance, bringing this innovative approach closer to routine clinical practice [88].

9.4 Role in Immunotherapy and Vaccine Development

Proteomics plays a crucial role in characterizing tumor antigens, neoantigens, and immune checkpoint regulators, thereby serving as a foundation for the development and optimization of immunotherapies and cancer vaccines. One of the key contributions of proteomics is HLA-peptidomics, which enables the identification of presented neoantigens that can be targeted by personalized cancer vaccines. Additionally, mapping the tumor immunopeptidome helps inform the selection of immune checkpoint inhibitors (ICIs), while monitoring cytokine profiles, immune cell proteomes, and immune-suppressive factors such as IDO1, TGF-β, and PD-L1 provides deeper insight into the tumor immune microenvironment [89]. Proteomic studies have demonstrated the predictive value of protein expression markers like PD-L1 and LAG3 for ICI response. Furthermore, tumor-associated antigens (TAAs) such as MAGE-A3 and NY-ESO-1, identified through proteomic analyses, have been used in peptide vaccine trials. Mass spectrometry-based immunopeptidomics has also been employed to tailor neoantigen-based vaccines in cancers like melanoma and glioblastoma, enhancing the precision and efficacy of these treatments [90, 91].

CONCLUSION

Proteomics has emerged as a powerful tool in advancing personalized cancer therapy by offering dynamic insights into tumor behavior that go beyond genomic information. Through advanced technologies such as mass spectrometry, protein microarrays, and phosphoproteomics, proteomics enables precise biomarker discovery, early cancer detection, patient stratification, and therapeutic target identification. The integration of proteomics with genomics and artificial intelligence has strengthened its clinical relevance, improving diagnosis, monitoring, and treatment outcomes across various cancer types. Despite existing challenges in data standardization and clinical translation, ongoing innovations are rapidly transforming proteomics into a cornerstone of precision oncology.

REFERENCE

1. Ibekwe PM, Akintayo EA, Okuku CN, Muhammed I, Jeje FM, Oseghale O, Ademola KO, Badru MD, Onwuemelem LA. Decoding Tumor Heterogeneity through Multi Omics: Insights into Cancer Evolution, Microenvironment and Therapy Resistance. Journal of Cancer and Tumor International. 2025 Jul 7;15(3):91-112.
2. Khoury R, Raffoul C, Khater C, Hanna C. Precision Medicine in Hematologic Malignancies: Evolving Concepts and Clinical Applications. Biomedicines. 2025 Jul 7;13(7):1654.
3. Guedes J, Woldmar N, Szasz AM, Wieslander E, Pawłowski K, Horvatovich P, Malm J, Szadai L, Németh IB, Marko-Varga G, Gil J. A perspective on integrating digital pathology, proteomics, clinical data and AI analytics in cancer research. Journal of proteomics. 2025 Jul 16:105493.
4. Makinde M. AI-Powered Biomarker Discovery for Personalized Oncology Drug Repurposing.
5. Gout J, Ekizce M, Roger E, Kleger A. Pancreatic organoids as cancer avatars for true personalized medicine. Advanced Drug Delivery Reviews. 2025 Jun 27:115642.
6. De Nicoló V, Frasca M, Graziosi A, Gazzaniga G, Torre DL, Pani A. Synthetic data generation in genomic cancer medicine: a review of global research trends in the last ten years. Discover Artificial Intelligence. 2025 Jul 15;5(1):148.
7. Chen Y, Fan AW, Huang L. Post-Translational Modifications (PTMs) in Human Cancer: Pharmacological Insights and Therapeutic Opportunities. Frontiers in Pharmacology. 2025 Jul 7; 16:1654659.
8. Gao Y, Qi F, Zhou W, Jiang P, Hu M, Wang Y, Song C, Han Y, Li D, Qin N, Zhang H. Liquid biopsy using plasma proteomics in predicting efficacy and tolerance of PD-1/PD-L1 blockades in NSCLC: a prospective exploratory study. Molecular Biomedicine. 2025 Jul 15;6(1):51.
9. Dominiak A, Chełstowska B, Nowicka G. Metabolic Adaptations in Cancer Progression: Optimization Strategies and Therapeutic Targets. Cancers. 2025 Jul 15;17(14):2341.
10. Aebersold R, Mann M. Mass-spectrometric exploration of proteome structure and function. Nature. 2016 Sep 15;537(7620):347-55.
11. Chen Y, Fan AW, Huang L. Post-Translational Modifications (PTMs) in Human Cancer: Pharmacological Insights and Therapeutic Opportunities. Frontiers in Pharmacology. 2025 Jul 7; 16:1654659.
12. Guedes J, Woldmar N, Szasz AM, Wieslander E, Pawłowski K, Horvatovich P, Malm J, Szadai L, Németh IB, Marko-Varga G, Gil J. A perspective on integrating digital pathology, proteomics, clinical data and AI analytics in cancer research. Journal of proteomics. 2025 Jul 16:105493.
13. Zhang B, Wang J, Wang X, Zhu J, Liu Q, Shi Z, Chambers MC, Zimmerman LJ, Shaddox KF, Kim S, Davies SR. Proteogenomic characterization of human colon and rectal cancer. Nature. 2014 Sep 18;513(7518):382-7.
14. Zhang H, Liu T, Zhang Z, Payne SH, Zhang B, McDermott JE, Zhou JY, Petyuk VA, Chen L, Ray D, Sun S. Integrated proteogenomic characterization of human high-grade serous ovarian cancer. Cell. 2016 Jul 28;166(3):755-65.
15. Rabilloud T. Two-dimensional gel electrophoresis in proteomics: old, old fashioned, but it still climbs up the mountains. PROTEOMICS: International Edition. 2002 Jan;2(1):3-10.
16. Zhu H, Snyder M. Protein chip technology. Current opinion in chemical biology. 2003 Feb 1;7(1):55-63.
17. Dominiak A, Chełstowska B, Nowicka G. Metabolic Adaptations in Cancer Progression: Optimization Strategies and Therapeutic Targets. Cancers. 2025 Jul 15;17(14):2341.
18. De Nicoló V, Frasca M, Graziosi A, Gazzaniga G, Torre DL, Pani A. Synthetic data generation in genomic cancer medicine: a review of global research trends in the last ten years. Discover Artificial Intelligence. 2025 Jul 15;5(1):148.
19. Yasar S, Melekoglu R. Proteomic Alterations in Ovarian Cancer: Predicting Residual Disease Status Using Artificial Intelligence and SHAP-Based Biomarker Interpretation. Frontiers in Medicine.;12:1562558.
20. Garraway LA, Verweij J, Ballman KV. Precision oncology: an overview. Journal of Clinical Oncology. 2013 May 20;31(15):1803-5.
21. Khoury R, Raffoul C, Khater C, Hanna C. Precision Medicine in Hematologic Malignancies: Evolving Concepts and Clinical

Applications. Biomedicines. 2025 Jul 7;13(7):1654.
22. Aebersold R, Mann M. Mass-spectrometric exploration of proteome structure and function. Nature. 2016 Sep 15;537(7620):347-55.
23. Zhang H, Liu T, Zhang Z, Payne SH, Zhang B, McDermott JE, Zhou JY, Petyuk VA, Chen L, Ray D, Sun S. Integrated proteogenomic characterization of human high-grade serous ovarian cancer. Cell. 2016 Jul 28;166(3):755-65.
24. Chen Y, Fan AW, Huang L. Post-Translational Modifications (PTMs) in Human Cancer: Pharmacological Insights and Therapeutic Opportunities. Frontiers in Pharmacology. 2025 Jul 7; 16:1654659.
25. Guedes J, Woldmar N, Szasz AM, Wieslander E, Pawłowski K, Horvatovich P, Malm J, Szadai L, Németh IB, Marko-Varga G, Gil J. A perspective on integrating digital pathology, proteomics, clinical data and AI analytics in cancer research. Journal of proteomics. 2025 Jul 16:105493.
26. Dominiak A, Chełstowska B, Nowicka G. Metabolic Adaptations in Cancer Progression: Optimization Strategies and Therapeutic Targets. Cancers. 2025 Jul 15;17(14):2341.
27. De Nicoló V, Frasca M, Graziosi A, Gazzaniga G, Torre DL, Pani A. Synthetic data generation in genomic cancer medicine: a review of global research trends in the last ten years. Discover Artificial Intelligence. 2025 Jul 15;5(1):148.
28. Gao Y, Qi F, Zhou W, Jiang P, Hu M, Wang Y, Song C, Han Y, Li D, Qin N, Zhang H. Liquid biopsy using plasma proteomics in predicting efficacy and tolerance of PD-1/PD-L1 blockades in NSCLC: a prospective exploratory study. Molecular Biomedicine. 2025 Jul 15;6(1):51.
29. Yasar S, Melekoglu R. Proteomic Alterations in Ovarian Cancer: Predicting Residual Disease Status Using Artificial Intelligence and SHAP-Based Biomarker Interpretation. Frontiers in Medicine.;12:1562558.
30. Zhang B, Wang J, Wang X, Zhu J, Liu Q, Shi Z, Chambers MC, Zimmerman LJ, Shaddox KF, Kim S, Davies SR. Proteogenomic characterization of human colon and rectal cancer. Nature. 2014 Sep 18;513(7518):382-7.
31. Dominiak A, Chełstowska B, Nowicka G. Metabolic Adaptations in Cancer Progression: Optimization Strategies and Therapeutic Targets. Cancers. 2025 Jul 15;17(14):2341.
32. Guedes J, Woldmar N, Szasz AM, Wieslander E, Pawłowski K, Horvatovich P, Malm J, Szadai L, Németh IB, Marko-Varga G, Gil J. A perspective on integrating digital pathology, proteomics, clinical data and AI analytics in cancer research. Journal of proteomics. 2025 Jul 16:105493.
33. Aebersold R, Mann M. Mass-spectrometric exploration of proteome structure and function. Nature. 2016 Sep 15;537(7620):347-55.
34. Zhang H, Liu T, Zhang Z, Payne SH, Zhang B, McDermott JE, Zhou JY, Petyuk VA, Chen L, Ray D, Sun S. Integrated proteogenomic characterization of human high-grade serous ovarian cancer. Cell. 2016 Jul 28;166(3):755-65.
35. Jung WH, Yam N, Chen CC, Elawad K, Hu B, Chen Y. Force-dependent extracellular matrix remodeling by early-stage cancer cells alters diffusion and induces carcinoma-associated fibroblasts. Biomaterials. 2020 Mar 1; 234:119756.
36. Yasar S, Melekoglu R. Proteomic Alterations in Ovarian Cancer: Predicting Residual Disease Status Using Artificial Intelligence and SHAP-Based Biomarker Interpretation. Frontiers in Medicine.;12:1562558.
37. De Nicoló V, Frasca M, Graziosi A, Gazzaniga G, Torre DL, Pani A. Synthetic data generation in genomic cancer medicine: a review of global research trends in the last ten years. Discover Artificial Intelligence. 2025 Jul 15;5(1):148.
38. Mertins P, Mani DR, Ruggles KV, Gillette MA, Clauser KR, Wang P, Wang X, Qiao JW, Cao S, Petralia F, Kawaler E. Proteogenomics connects somatic mutations to signalling in breast cancer. Nature. 2016 Jun 2;534(7605):55-62.
39. Gao Y, Qi F, Zhou W, Jiang P, Hu M, Wang Y, Song C, Han Y, Li D, Qin N, Zhang H. Liquid biopsy using plasma proteomics in predicting efficacy and tolerance of PD-1/PD-L1 blockades in NSCLC: a prospective exploratory study. Molecular Biomedicine. 2025 Jul 15;6(1):51.
40. Wang N, Wang R, Li X, Song Z, Xia L, Wang J, Zhang L, Wu A, Ding Z. Tumor microenvironment profiles reveal distinct therapy-oriented proteogenomic characteristics in colorectal cancer. Frontiers in Bioengineering and Biotechnology. 2021 Oct 28; 9:757378.

41. Brigham & Women's Hospital & Harvard Medical School Chin Lynda 9 11 Park Peter J. 12 Kucherlapati Raju 13, Genome data analysis: Baylor College of Medicine Creighton Chad J. 22 23 Donehower Lawrence A. 22 23 24 25, Institute for Systems Biology Reynolds Sheila 31 Kreisberg Richard B. 31 Bernard Brady 31 Bressler Ryan 31 Erkkila Timo 32 Lin Jake 31 Thorsson Vesteinn 31 Zhang Wei 33 Shmulevich Ilya 31, Oregon Health & Science University Anur Pavana 37 Spellman Paul T. 37. Comprehensive molecular portraits of human breast tumours. Nature. 2012 Oct 4;490(7418):61-70.
42. Honaker Y, Hubbard N, Xiang Y, Fisher L, Hagin D, Sommer K, Song Y, Yang SJ, Lopez C, Tappen T, Dam EM. Gene editing to induce FOXP3 expression in human CD4+ T cells leads to a stable regulatory phenotype and function. Science translational medicine. 2020 Jun 3;12(546): eaay6422.
43. Pourakbar N, Motamedi A, Pashapour M, Sharifi ME, Sharabiani SS, Fazlollahi A, Abdollahi H, Rahmim A, Rezaei S. Effectiveness of Artificial Intelligence Models in Predicting Lung Cancer Recurrence: A Gene Biomarker-Driven Review. Cancers. 2025 Jun 5;17(11):1892.
44. Zhang H, Liu T, Zhang Z, Payne SH, Zhang B, McDermott JE, Zhou JY, Petyuk VA, Chen L, Ray D, Sun S. Integrated proteogenomic characterization of human high-grade serous ovarian cancer. Cell. 2016 Jul 28;166(3):755-65.
45. Jaglowski JR, Stack BC, Madhava K, Hartley A, Wake M, Watkinson JC, Glaholm J. Bibliography Current World Literature Vol 19 No 3 May 2007. cancer. 2006;64(1308).
46. Aebersold R, Mann M. Mass-spectrometric exploration of proteome structure and function. Nature. 2016 Sep 15;537(7620):347-55.
47. Zhang B, Wang J, Wang X, Zhu J, Liu Q, Shi Z, Chambers MC, Zimmerman LJ, Shaddox KF, Kim S, Davies SR. Proteogenomic characterization of human colon and rectal cancer. Nature. 2014 Sep 18;513(7518):382-7.
48. Mertins P, Mani DR, Ruggles KV, Gillette MA, Clauser KR, Wang P, Wang X, Qiao JW, Cao S, Petralia F, Kawaler E. Proteogenomics connects somatic mutations to signalling in breast cancer. Nature. 2016 Jun 2;534(7605):55-62.
49. Franken H, Mathieson T, Childs D, Sweetman GM, Werner T, Tögel I, Doce C, Gade S, Bantscheff M, Drewes G, Reinhard FB. Thermal proteome profiling for unbiased identification of direct and indirect drug targets using multiplexed quantitative mass spectrometry. Nature protocols. 2015 Oct;10(10):1567-93.
50. Jean Beltran PM, Federspiel JD, Sheng X, Cristea IM. Proteomics and integrative omic approaches for understanding host–pathogen interactions and infectious diseases. Molecular systems biology. 2017 Mar;13(3):922.
51. Akbani R, Ng PK, Werner HM, Shahmoradgoli M, Zhang F, Ju Z, Liu W, Yang JY, Yoshihara K, Li J, Ling S. A pan-cancer proteomic perspective on The Cancer Genome Atlas. Nature communications. 2014 May 29;5(1):3887.
52. Becher I, Werner T, Doce C, Zaal EA, Tögel I, Khan CA, Rueger A, Muelbaier M, Salzer E, Berkers CR, Fitzpatrick PF. Thermal profiling reveals phenylalanine hydroxylase as an off-target of panobinostat. Nature chemical biology. 2016 Nov;12(11):908-10.
53. Brigham & Women's Hospital & Harvard Medical School Chin Lynda 9 11 Park Peter J. 12 Kucherlapati Raju 13, Genome data analysis: Baylor College of Medicine Creighton Chad J. 22 23 Donehower Lawrence A. 22 23 24 25, Institute for Systems Biology Reynolds Sheila 31 Kreisberg Richard B. 31 Bernard Brady 31 Bressler Ryan 31 Erkkila Timo 32 Lin Jake 31 Thorsson Vesteinn 31 Zhang Wei 33 Shmulevich Ilya 31, Oregon Health & Science University Anur Pavana 37 Spellman Paul T. 37. Comprehensive molecular portraits of human breast tumours. Nature. 2012 Oct 4;490(7418):61-70.
54. Turner NC, Ro J, André F, Loi S, Verma S, Iwata H, Harbeck N, Loibl S, Huang Bartlett C, Zhang K, Giorgetti C. Palbociclib in hormone-receptor–positive advanced breast cancer. New England Journal of Medicine. 2015 Jul 16;373(3):209-19.
55. Gao Y, Qi F, Zhou W, Jiang P, Hu M, Wang Y, Song C, Han Y, Li D, Qin N, Zhang H. Liquid biopsy using plasma proteomics in predicting efficacy and tolerance of PD-1/PD-L1 blockades in NSCLC: a prospective exploratory study. Molecular Biomedicine. 2025 Jul 15;6(1):51.

56. Wang N, Wang R, Li X, Song Z, Xia L, Wang J, Zhang L, Wu A, Ding Z. Tumor microenvironment profiles reveal distinct therapy-oriented proteogenomic characteristics in colorectal cancer. Frontiers in Bioengineering and Biotechnology. 2021 Oct 28; 9:757378.
57. Zhang H, Liu T, Zhang Z, Payne SH, Zhang B, McDermott JE, Zhou JY, Petyuk VA, Chen L, Ray D, Sun S. Integrated proteogenomic characterization of human high-grade serous ovarian cancer. Cell. 2016 Jul 28;166(3):755-65.
58. Jaglowski JR, Stack BC, Madhava K, Hartley A, Wake M, Watkinson JC, Glaholm J. Bibliography Current World Literature Vol 19 No 3 May 2007. cancer. 2006;64(1308).
59. Aebersold R, Mann M. Mass-spectrometric exploration of proteome structure and function. Nature. 2016 Sep 15;537(7620):347-55.
60. Mertins P, Mani DR, Ruggles KV, Gillette MA, Clauser KR, Wang P, Wang X, Qiao JW, Cao S, Petralia F, Kawaler E. Proteogenomics connects somatic mutations to signalling in breast cancer. Nature. 2016 Jun 2;534(7605):55-62.
61. Shi H, Hugo W, Kong X, Hong A, Koya RC, Moriceau G, Chodon T, Guo R, Johnson DB, Dahlman KB, Kelley MC. Acquired resistance and clonal evolution in melanoma during BRAF inhibitor therapy. Cancer discovery. 2014 Jan 1;4(1):80-93.
62. De Nicoló V, Frasca M, Graziosi A, Gazzaniga G, Torre DL, Pani A. Synthetic data generation in genomic cancer medicine: a review of global research trends in the last ten years. Discover Artificial Intelligence. 2025 Jul 15;5(1):148.
63. Li J, Zhao W, Akbani R, Liu W, Ju Z, Ling S, Vellano CP, Roebuck P, Yu Q, Eterovic AK, Byers LA. Characterization of human cancer cell lines by reverse-phase protein arrays. Cancer cell. 2017 Feb 13;31(2):225-39.
64. Khoury R, Raffoul C, Khater C, Hanna C. Precision Medicine in Hematologic Malignancies: Evolving Concepts and Clinical Applications. Biomedicines. 2025 Jul 7;13(7):1654.
65. Mansinho A, Boni V, Miguel M, Calvo E. New designs in early clinical drug development. Annals of Oncology. 2019 Sep 1;30(9):1460-5.
66. Yasar S, Melekoglu R. Proteomic Alterations in Ovarian Cancer: Predicting Residual Disease Status Using Artificial Intelligence and SHAP-Based Biomarker Interpretation. Frontiers in Medicine.;12:1562558.
67. Gao Y, Qi F, Zhou W, Jiang P, Hu M, Wang Y, Song C, Han Y, Li D, Qin N, Zhang H. Liquid biopsy using plasma proteomics in predicting efficacy and tolerance of PD-1/PD-L1 blockades in NSCLC: a prospective exploratory study. Molecular Biomedicine. 2025 Jul 15;6(1):51.
68. Dominiak A, Chełstowska B, Nowicka G. Metabolic Adaptations in Cancer Progression: Optimization Strategies and Therapeutic Targets. Cancers. 2025 Jul 15;17(14):2341.
69. Li J, Zhao W, Akbani R, Liu W, Ju Z, Ling S, Vellano CP, Roebuck P, Yu Q, Eterovic AK, Byers LA. Characterization of human cancer cell lines by reverse-phase protein arrays. Cancer cell. 2017 Feb 13;31(2):225-39.
70. Yasar S, Melekoglu R. Proteomic Alterations in Ovarian Cancer: Predicting Residual Disease Status Using Artificial Intelligence and SHAP-Based Biomarker Interpretation. Frontiers in Medicine.;12:1562558.
71. Zhang H, Liu T, Zhang Z, Payne SH, Zhang B, McDermott JE, Zhou JY, Petyuk VA, Chen L, Ray D, Sun S. Integrated proteogenomic characterization of human high-grade serous ovarian cancer. Cell. 2016 Jul 28;166(3):755-65.
72. Li Y, Dou Y, Leprevost FD, Geffen Y, Calinawan AP, Aguet F, Akiyama Y, Anand S, Birger C, Cao S, Chaudhary R. Proteogenomic data and resources for pan-cancer analysis. Cancer cell. 2023 Aug 14;41(8):1397-406.
73. Wolff AC, Hammond ME, Allison KH, Harvey BE, Mangu PB, Bartlett JM, Bilous M, Ellis IO, Fitzgibbons P, Hanna W, Jenkins RB. Human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline focused update. Archives of pathology & laboratory medicine. 2018 Nov 1;142(11):1364-82.
74. Jordan HA, Thomas SN. Novel proteomic technologies to address gaps in pre-clinical ovarian cancer biomarker discovery efforts. Expert Review of Proteomics. 2023 Dec 2;20(12):439-50.
75. Tabb DL, Vega-Montoto L, Rudnick PA, Variyath AM, Ham AJ, Bunk DM, Kilpatrick LE,

Billheimer DD, Blackman RK, Cardasis HL, Carr SA. Repeatability and reproducibility in proteomic identifications by liquid chromatography− tandem mass spectrometry. Journal of proteome research. 2010 Feb 5;9(2):761-76.

76. Aebersold R, Mann M. Mass-spectrometric exploration of proteome structure and function. Nature. 2016 Sep 15;537(7620):347-55.
77. MacLean B, Tomazela DM, Shulman N, Chambers M, Finney GL, Frewen B, Kern R, Tabb DL, Liebler DC, MacCoss MJ. Skyline: an open source document editor for creating and analyzing targeted proteomics experiments. Bioinformatics. 2010 Apr 1;26(7):966-8.
78. Collins BC, Hunter CL, Liu Y, Schilling B, Rosenberger G, Bader SL, Chan DW, Gibson BW, Gingras AC, Held JM, Hirayama-Kurogi M. Multi-laboratory assessment of reproducibility, qualitative and quantitative performance of SWATH-mass spectrometry. Nature communications. 2017 Aug 21;8(1):291.
79. Poste G. Bring on the biomarkers. Nature. 2011 Jan 13;469(7329):156-7.
80. De Nicoló V, Frasca M, Graziosi A, Gazzaniga G, Torre DL, Pani A. Synthetic data generation in genomic cancer medicine: a review of global research trends in the last ten years. Discover Artificial Intelligence. 2025 Jul 15;5(1):148.
81. Li Y, Dou Y, Leprevost FD, Geffen Y, Calinawan AP, Aguet F, Akiyama Y, Anand S, Birger C, Cao S, Chaudhary R. Proteogenomic data and resources for pan-cancer analysis. Cancer cell. 2023 Aug 14;41(8):1397-406.
82. Hasin Y, Seldin M, Lusis A. Multi-omics approaches to disease. Genome biology. 2017 May 5;18(1):83.
83. Zhang B, Wang J, Wang X, Zhu J, Liu Q, Shi Z, Chambers MC, Zimmerman LJ, Shaddox KF, Kim S, Davies SR. Proteogenomic characterization of human colon and rectal cancer. Nature. 2014 Sep 18;513(7518):382-7.
84. De Nicoló V, Frasca M, Graziosi A, Gazzaniga G, Torre DL, Pani A. Synthetic data generation in genomic cancer medicine: a review of global research trends in the last ten years. Discover Artificial Intelligence. 2025 Jul 15;5(1):148.
85. Budnik B, Levy E, Harmange G, Slavov N. SCoPE-MS: mass spectrometry of single mammalian cells quantifies proteome heterogeneity during cell differentiation. Genome biology. 2018 Oct 22;19(1):161.
86. Cheung TK, Lee CY, Bayer FP, McCoy A, Kuster B, Rose CM. Defining the carrier proteome limit for single-cell proteomics. Nature Methods. 2021 Jan;18(1):76-83.
87. Dominiak A, Chełstowska B, Nowicka G. Metabolic Adaptations in Cancer Progression: Optimization Strategies and Therapeutic Targets. Cancers. 2025 Jul 15;17(14):2341.
88. Gao Y, Qi F, Zhou W, Jiang P, Hu M, Wang Y, Song C, Han Y, Li D, Qin N, Zhang H. Liquid biopsy using plasma proteomics in predicting efficacy and tolerance of PD-1/PD-L1 blockades in NSCLC: a prospective exploratory study. Molecular Biomedicine. 2025 Jul 15;6(1):51.
89. Ott PA, Hu Z, Keskin DB, Shukla SA, Sun J, Bozym DJ, Zhang W, Luoma A, Giobbie-Hurder A, Peter L, Chen C. An immunogenic personal neoantigen vaccine for patients with melanoma. Nature. 2017 Jul 13;547(7662):217-21.
90. Sahin U, Derhovanessian E, Miller M, Kloke BP, Simon P, Löwer M, Bukur V, Tadmor AD, Luxemburger U, Schrörs B, Omokoko T. Personalized RNA mutanome vaccines mobilize poly-specific therapeutic immunity against cancer. Nature. 2017 Jul 13;547(7662):222-6.
91. Carreno BM, Magrini V, Becker-Hapak M, Kaabinejadian S, Hundal J, Petti AA, Ly A, Lie WR, Hildebrand WH, Mardis ER, Linette GP. A dendritic cell vaccine increases the breadth and diversity of melanoma neoantigen-specific T cells. Science. 2015 May 15;348(6236):803-8.

HOW TO CITE: Ishwari Jaiswal*, Ruturaj Kulkarni, Garima Singh, Vaishnavi Rindhe, Krutika Patil, Proteomics in Personalized Cancer Therapy: Advances, Applications, and Future Perspectives, Int. J. Sci. R. Tech., 2025, 2 (8), 127-146. https://doi.org/10.5281/zenodo.16810308