World Journal of Surgical Oncology

REVIEW

Open Access

New genomic and proteomic biomarker discovery in cancer: revolutionizing diagnosis and prognostication

Monika Rajput[1,2], Manoj Pandey[1,2,3] and Ruhi Dixit[3*]

Abstract

Cancer remains a major global health challenge, with substantial morbidity and mortality worldwide. Advances in genomic and proteomic biomarker discovery have transformed cancer diagnosis, prognosis, and treatment selection. The evolution from early serological markers such as carcinoembryonic antigen (CEA) and prostate-specific antigen (PSA) to modern multi-omics approaches enabled by next-generation sequencing (NGS), mass spectrometry (MS), and advanced bioinformatics has revolutionized personalized medicine and targeted therapy, leading to improved outcomes. This review highlights the historical evolution of cancer biomarkers and the current landscape of genomic, proteomic, and proteogenomic biomarkers. We emphasize the role of liquid biopsies, artificial intelligence (AI), and integrative multi-omics analytics in accelerating biomarker identification and validation. We also discuss the differential pace of clinical adoption in high-income versus low- and middle-income countries (LMICs), and outline ongoing challenges including tumor heterogeneity, standardization, cost, and regulatory barriers. Despite these limitations, recent innovations in multi-omics technologies and AI-driven analysis promise to further advance precision oncology and enable more equitable, personalized cancer care worldwide.

Keywords Cancer, Genomic, Proteomic, Biomarkers, Bioinformatics, Multi-omics, Artificial intelligence

Background

Cancer continues to be a major global health burden, with approximately 20 million new cases and 9.7 million deaths reported worldwide in 2022, according to the GLOBOCAN 2022 publication [1]. The intricate heterogeneity of cancer has long challenged early detection, accurate diagnosis, and effective treatment. Over the past few decades, the rise of genomic and proteomic biomarker discovery, driven by advancements in bioinformatics and open-access data repositories, has reshaped the oncology landscape, enabling precision medicine.

This review on "New Genomic and Proteomic Biomarker Discovery in Cancer" traces the historical evolution, development, and validation of genomic and proteomic biomarkers, emphasizing how scientific progress, technological innovations, bioinformatics, and open-access data have driven their identification and how these biomarkers have transformed cancer diagnosis and prognostication, improving patient outcomes. We further examine how these biomarkers are transforming cancer diagnosis and prognostication, and explore practical considerations for implementing such technologies

*Correspondence:
Ruhi Dixit
ruhi.dixit3@bhu.ac.in
[1]DHR-ICMR Advanced Molecular Oncology Diagnostic Services (DIAMOnDS), Institute of Medical Sciences, Banaras Hindu University, Varanasi 221,005, India
[2]Department of Surgical Oncology, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221,005, India
[3]Health Technology Assessment India (HTAIn) resource centre, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221,005, India

in diverse health systems, including low- and middle-income countries (LMICs).

Added value of the study

While recent reviews have explored the latest advances in multi-omics technologies, this article specifically integrates discoveries in genomics, proteomics, and proteogenomics with a focus on their clinical readiness, regulatory status, and global implementation gaps. We pay particular attention to the unique barriers and opportunities in LMICs, where factors like limited infrastructure, higher costs, and workforce gaps affect how new technologies are adopted. This review further compares the strengths and weaknesses of methods such as next-generation sequencing, mass spectrometry, liquid biopsy, and AI-driven biomarker tools. It also covers the most recent findings from major research projects like The Cancer Genome Atlas (TCGA) and the Clinical Proteomic Tumor Analysis Consortium (CPTAC), as well as developments in AI-assisted prediction, to provide a practical, globally relevant perspective on how biomarkers are discovered and validated for clinical use.

Historical evolution of cancer biomarkers

The concept of cancer biomarkers, i.e. molecular indicators of a biological state linked to malignancy, emerged in the mid-20th century. Early biomarkers were serological, such as carcinoembryonic antigen (CEA), identified in 1965 for colorectal cancer [2]. CEA became vital for monitoring disease progression and treatment response, though its limited specificity constrained its diagnostic utility. Prostate-specific antigen (PSA), introduced in the 1980s, revolutionized prostate cancer screening, contributing to a significant decline in mortality [3]. However, PSA's issues with false positives and over diagnosis underscored the need for more precise biomarkers.

The 1970s and 1980s marked a turning point with the discovery of oncogenes and tumor suppressor genes. In 1979, p53 was identified as a key tumor suppressor, mutated in over half of cancers [4]. The cloning of the retinoblastoma (Rb) gene in 1986 and the identification of HRAS and KRAS oncogenes in the early 1980s laid the foundation for genomic biomarkers [5, 6]. These discoveries facilitated targeted therapies, such as the KRASG12C inhibitor sotorasib, approved by the FDA in 2021 for non-small cell lung cancer (NSCLC) [7].

The 1990s brought hereditary cancer biomarkers, with BRCA1 and BRCA2 mutations linked to elevated risks of breast and ovarian cancers [8, 9]. These findings enabled risk assessment and preventive strategies, including prophylactic surgeries and PARP inhibitors. Concurrently, advances in monoclonal antibodies and immunoassays transformed proteomic biomarker research by enabling detection of targetable cancer-associated proteins.

The early 2000s introduced high-throughput technologies, such as DNA microarrays and next-generation sequencing (NGS), which allowed comprehensive gene expression analysis [10]. Proteomics advanced with mass spectrometry (MS)-based techniques, identifying cancer-related proteins and peptides [11]. The rise of bioinformatics and open-access data repositories further accelerated biomarker discovery by enabling large-scale data analysis and sharing. These developments set the stage for multi-omics approaches integrating genomics, transcriptomics, proteomics, and metabolomics (Fig. 1).

Genomic biomarkers

Genomic biomarkers include DNA-based alterations, such as mutations, copy number variations, and epigenetic changes, as well as RNA-based markers like microRNAs (miRNAs) and long non-coding RNAs (lncRNAs). Next-generation sequencing (NGS) has been pivotal in identifying these biomarkers. Whole-exome sequencing (WES) and whole-genome sequencing (WGS) have uncovered driver mutations, such as EGFR mutations in NSCLC and BRAF V600E in melanoma, p53 and RAS mutations in head neck cancer guiding targeted therapies like EGFR and BRAF inhibitors [12–14]. RNA sequencing (RNAseq) has broadened the scope of genomic biomarkers by identifying gene expression profiles and non-coding RNAs [15, 16]. The Oncotype DX assay, analyzing 16 genes in breast cancer, predicts recurrence risk and informs chemotherapy decisions [17]. MammaPrint, a 70-gene signature, stratifies breast cancer patients into low- and high-risk recurrence groups [18]. These assays, although clinically established, are single-omics transcriptomic tests and do not integrate additional molecular layers.

RNA sequencing has expanded the discovery of transcriptomic biomarkers, including gene expression signatures and non-coding RNAs. In gliomas, prognostic biomarkers such as IDH1/IDH2 mutations are identified through DNA sequencing rather than RNA-seq, and remain among the most clinically relevant genomic alterations associated with improved survival [19]. Despite significant technological advancements, biomarker development has faced several historical and ongoing challenges. Genomic biomarkers may suffer from tumor heterogeneity and sampling bias, leading to discordant results across tissue and liquid modalities.

Liquid biopsies, analyzing circulating tumor DNA (ctDNA), cell-free DNA (cfDNA), and circulating tumor cells (CTCs) in blood or biofluids, offer a non-invasive approach to genomic biomarker discovery. These tests enable real-time tumor monitoring, minimal residual disease detection, and identification of resistance mutations, such as EGFR T790M in NSCLC, which predicts response to osimertinib [20]. The FDA approval of liquid

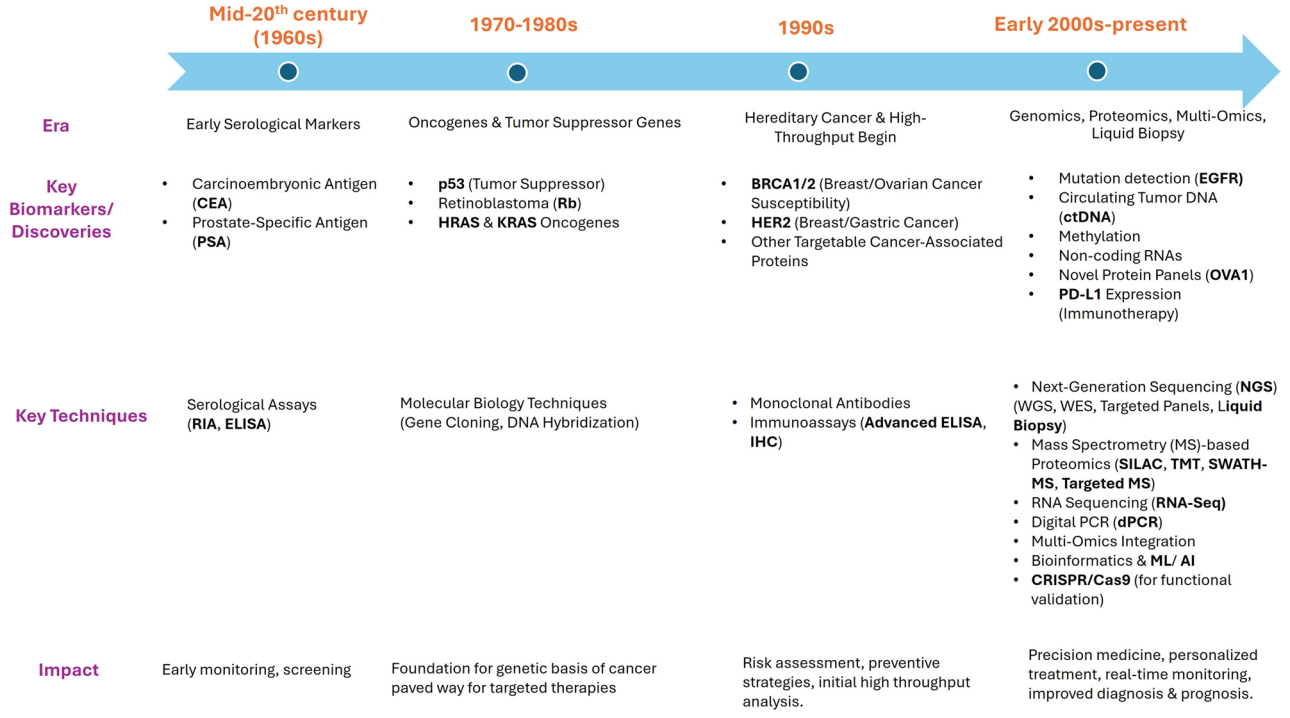

Fig. 1 Development of genomic and proteomic biomarkers. Historical evolution of cancer biomarker discovery and detection techniques. [The figure illustrates significant milestones and technological advancements that have accelerated biomarker research]

biopsy tests like Guardant360 CDx and FoundationOne Liquid CDx highlights their clinical value [21]. Liquid biopsies help in tumors where getting the tumor tissue is difficult due to anatomic reasons such as lung and gallbladder cancer or where the tumor responds to neoadjuvant therapy like breast cancer, and it is where these techniques has been found to be most useful. However, liquid biopsy also exhibits variable sensitivity due to tumor shedding differences across cancer types. Early-stage cancers, gliomas, and certain indolent tumors often release insufficient ctDNA for reliable detection. Additionally, clonal hematopoiesis of indeterminate potential (CHIP) may introduce false positives, complicating interpretation. While genomic biomarkers remain foundational in oncology, their ability to predict outcomes is increasingly being enhanced or complemented by transcriptomic, proteomic, and epigenomic signatures.

Proteomic biomarkers

Proteomic biomarkers encompass proteins, peptides, and post-translational modifications (PTMs) reflecting cancer cell function. The human proteome, estimated at 500,000 proteins from approximately 35,000 genes, is highly complex due to alternative splicing and PTMs [22]. Mass spectrometry-based proteomics, including stable isotope labeling by amino acids in cell culture (SILAC), tandem mass tags (TMT), and sequential window acquisition of all theoretical fragment ion spectra (SWATH-MS), has enabled high-throughput protein analysis [23–25]. Emerging areas such as single-cell proteomics provide unprecedented resolution of intra-tumoral heterogeneity, revealing resistant cellular subpopulations and therapy-induced phenotypes.

Proteomic studies have identified clinically relevant biomarkers, such as the OVA1 assay for ovarian cancer, combining five proteins (CA125, prealbumin, apolipoprotein A1, beta-2-microglobulin, and transferrin) to assess malignancy risk [26]. Proteomic profiling of colorectal cancer tissues has revealed biomarkers like Mucin 5AC, linked to tumor invasiveness [27], in head neck cancers biomarkers like p53 antibodies, heat shock protein 70 etc., has been identified [28]. In hepatocellular carcinoma, SWATH-MS identified protein abundance changes as a prognostic biomarker tied to disease progression [29]. Clinical applications of proteomic biomarkers are expanding. Phospho-proteomic signatures, such as phospho-ERK and phospho-AKT patterns, are being evaluated as predictors of response to MEK and PI3K inhibitors in melanoma and lung cancers. Immunopeptidomics has identified clinically actionable neoantigens that have progressed into early-phase vaccine trials.

Proteogenomic, integrating proteomic and genomic data, has uncovered novel biomarkers. A lung adenocarcinoma study identified MCT1 and GLUT1 as prognostic markers, demonstrating the synergy between genomic and proteomic data [30]. Proteomic analysis of tumor secretomes and microenvironments has also revealed biomarkers like class III β-tubulin in ovarian cancer,

predicting poor survival in neoadjuvant chemotherapy patients [31].

Despite substantial progress, proteomic biomarker development is constrained by pre-analytical variability, batch effects, protein instability, and differences in MS platforms. The high dynamic range of plasma proteins, with abundant proteins masking low-abundance candidates, presents an ongoing analytical challenge. Standardization of sample processing, MS workflows, and data analysis is critical for reproducible, multi-center proteomic biomarker validation.

Validation of genomic and proteomic biomarkers

The transition from biomarker discovery to clinical use requires rigorous validation to ensure sensitivity, specificity, and reproducibility. Challenges include tumor heterogeneity, biological variability, and technical limitations like sample collection and analytical variability. The Early Detection Research Network (EDRN) at the National Cancer Institute has standardized validation protocols [32]. The development pipeline is shown in Fig. 2.

Genomic biomarker validation

Genomic biomarkers are validated through large-scale clinical trials and cohort studies. EGFR mutations, predictive of EGFR tyrosine kinase inhibitor response in NSCLC, were validated through multi-center trials showing improved progression-free survival [33]. The ClonoSEQ assay, the first FDA-approved NGS-based test for minimal residual disease in leukemia and multiple myeloma, was validated in extensive cohorts [34]. Challenges include NGS costs, platform standardization, and validating rare mutations due to limited cohorts. Sequential filtering and DNA pooling strategies enhance efficiency [35]. Open-access repositories like The Cancer Genome Atlas (TCGA) and cBioPortal facilitate validation by providing large genomic datasets [36].

Proteomic biomarker validation

Proteomic validation is hindered by the complexity of biological samples, such as blood, with a high dynamic range of protein concentrations. Techniques like surface-enhanced laser desorption/ionization (SELDI) and two-dimensional gel electrophoresis (2-DE) aid protein separation, followed by MS identification [37]. Orthogonal methods, such as enzyme-linked immunosorbent assay (ELISA) and Western blotting, confirm results. Challenges include abundant proteins obscuring low-abundance biomarkers. Multi-center studies with standardized protocols and targeted MS assays are essential [38].

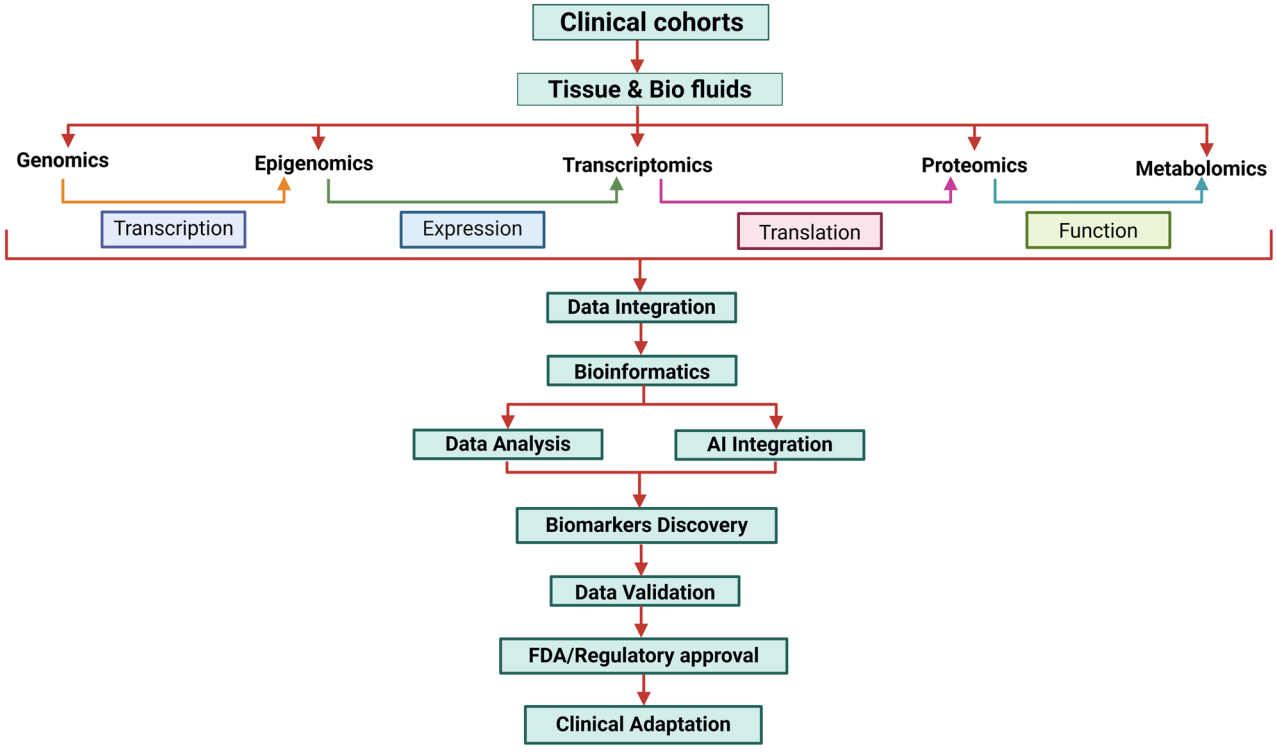

Fig. 2 Multi-omics workflow for biomarker discovery. [This image depicts the steps involved in integrating genomic, transcriptomic, proteomic, and metabolomic data to identify and validate potential biomarkers]

Technological advancements in biomarker discovery

The convergence of high-throughput molecular technologies and advanced computation has accelerated biomarker discovery. Table 1 below summarizes the key technologies that are driving the discovery of genomic and proteomic biomarkers. It gives a summary of the main platforms, their uses, and their significance in biomarker research.

Multi-omics biomarkers - clinical adoption vs. research-stage technologies

The integration of multiple molecular layers represents a paradigm shift beyond single-omics assays, enabling deeper biological insight and improved predictive power. Multi-omics technologies, including genomics, transcriptomics, proteomics, metabolomics, and epigenomics, have significantly accelerated biomarker discovery; however, their integration into routine clinical oncology still lags far behind their rapidly growing presence in research.

In contemporary practice, the majority of clinically implemented biomarkers continue to rely on targeted genomic sequencing, immunohistochemistry (PD-L1 expression), microsatellite instability (MSI) testing, and a small number of validated transcriptomic panels such as Oncotype DX and MammaPrint. In contrast, comprehensive multi-omics assays that integrate multiple molecular layers, such as combined transcriptomic–proteomic (proteogenomic) signatures, are still largely confined to exploratory or translational research settings.

Various multi-omics related tools that have progressed to clinical adoption include a limited number of validated assays that combine genomic and transcriptomic information for therapeutic decision-making. Most clinically implemented biomarker assays, are based solely on mRNA expression profiling and therefore represent single-omics transcriptomic assays, not multi-omics biomarkers. These include transcriptomic expression panels such as Oncotype DX (21-gene panel) and MammaPrint (70-gene signature), both of which guide adjuvant therapy decisions in early-stage breast cancer [45]. Similarly, homologous recombination deficiency (HRD) and BRCA deficiency assays integrate measures of genomic instability to help identify patients who may benefit from PARP inhibitor therapy [46]. In contrast, true multi-omics assays integrate at least two molecular layers - such as DNA + RNA, DNA + methylation, RNA + protein, or proteogenomic profiles. Clinically adopted multi-omics tests remain relatively few, but they represent a critical bridge between discovery-stage multi-omics research and routine precision oncology.

In the liquid biopsy domain, circulating tumor DNA (ctDNA) assays - including Guardant360 CDx and FoundationOne Liquid CDx - combine multiple molecular layers, such as sequence variants, copy-number alterations, and methylation features, to support molecular profiling when tissue biopsies are limited or infeasible [47]. Furthermore, clinical NGS-based diagnostic panels targeting 30–500 genes are now routinely used across oncology to detect actionable mutations, refine diagnosis, and inform targeted treatment strategies. Collectively, these examples represent the small subset of multi-omics-derived approaches that have achieved integration into routine clinical workflows. The assays listed in Table 2 represent the few platforms that integrate multi-layer molecular data and therefore qualify as true multi-omics biomarkers with emerging or established clinical relevance.

A structured search of ClinicalTrials.gov identified a total of 121 cancer-related clinical studies investigating multi-omics biomarkers (Table 3). These trials encompass a broad spectrum of applications, including early cancer detection, risk stratification, treatment-response prediction, surgical planning, and molecular or digital pathology - based decision support. Only 10 clinical trials were found to have reached full completion, demonstrating the most mature evidence base within this landscape. This compiled list highlights that, despite increasing interest, truly multi-omics clinical trials represent only a small fraction of ongoing biomarker research. Most registered trials remain in the recruitment or early-phase exploratory stage, underscoring the gap between technological capability and clinical translation.

Several barriers continue to hinder the widespread clinical adoption of multi-omics biomarkers. These include the high cost and specialized expertise required for mass spectrometry–based proteomics, limited standardization

Table 1 Key technologies driving biomarker discovery

Technology	Description	Impact on Biomarker Discovery
Next-Generation Sequencing (NGS)	Rapid sequencing of genomes, exomes, or gene panels	Identifies somatic mutations and epigenetic alterations in cancers like NSCLC [39]
Mass Spectrometry (MS)	High-throughput protein quantification using SILAC, TMT, and SWATH-MS	Enables single-cell proteomics and PTM detection [40]
Liquid Biopsies	Analysis of ctDNA, cfDNA, and CTCs in biofluids	Monitors tumor dynamics non-invasively [41]
Multi-Omics Integration	Combines genomics, transcriptomics, proteomics, and metabolomics	Uncovers novel biomarkers via holistic analysis [42]
Artificial Intelligence (AI)	Analyzes omics data using machine learning	Enhances diagnostic accuracy through pattern recognition [43]
CRISPR/Cas9	Gene editing for functional genomics	Validates biomarker function and targets [44]

Table 2 Clinically available multi-omics biomarker products and their molecular components

S. No.	Product Name	Molecular Layers (Multi-Omics)	Clinical Application	Regulatory Status	Key Reference
1	**FoundationOne® CDx** (Foundation Medicine / Roche)	DNA mutations, CNVs, gene fusions, MSI, TMB (Genomics + mutational signatures)	Tumor profiling; targeted therapy selection; For all solid tumors	**FDA-approved CDx**	[48]
2	**Guardant360® CDx** (Guardant Health)	cfDNA mutations, CNVs, fusion detection (Genomic liquid biopsy + fragmentomics)	Non-invasive tumor profiling; For advanced solid tumors	**FDA-approved CDx**	[49]
3	**Caris Molecular Intelligence®** (Caris Life Sciences)	DNA sequencing + RNA sequencing + protein/IHC + MSI/methylation	Comprehensive therapy selection and resistance profiling; For solid tumors	CLIA-certified multi-omics platform	[50]
4	**Tempus xT (500 + gene panel)**	DNA sequencing + RNA sequencing + AI-based fusion/expression analysis	Actionable mutation profiling; expression-based therapy markers; For solid tumors	CLIA/CAP-certified	[51]
5	**MSK-IMPACT® + MSK-Fusion RNA Panel**	DNA sequencing (IMPACT) + RNA-seq for fusions + MSI/TMB	Pan-cancer actionable molecular profiling; For solid tumors	FDA-recognized NYS test	[52]
6	**Galleri® MCED test (GRAIL)**	cfDNA methylation + fragmentation patterns + AI classifier (Epigenomics + computational multi-omics)	Multi-cancer early detection and tissue-of-origin prediction; screens for a "cancer signal" across over 50 types of cancer	LDT; large clinical trials	[53]
7	**ClonoSEQ® MRD Assay** (Adaptive Biotechnologies)	IGH/IGK/TRA immune receptor sequencing + Bayesian multi-omic modeling	Minimal residual disease (ALL, CLL, Multiple myeloma); lymphoid blood cancers	FDA-authorized	[54]
8	**Caris GPSai™ (AI Multi-Omics)**	DNA + RNA + Protein/IHC + clinical features integrated by AI	Predicts therapy response; tumor classification; For Cancer of Unknown Primary (CUP).	CLIA-certified	[55]
9	**ExoDx Prostate IntelliScore™**	EV-derived RNA signatures + cfRNA (Transcriptomic + EV proteomic context)	Predicts risk of high-grade prostate cancer	CLIA assay	[56]
10	**ThyroSeq® v3 (Thyroid cancer)**	DNA mutations, RNA fusions, copy-number alterations, expression markers	Indeterminate thyroid nodule classification	CLIA-approved	[57]

Table 3 List of clinical trials studies associated with multi-omics biomarkers

NCT Number	Study Title	Study Status	Interventions
NCT04972201	A Proof-of-Concept Study of Pan-cancer Early Detection by Liquid Biopsy	COMPLETED	DEVICE: Multi-cancer early detection test
NCT06969768	Proteogenomics for Follicular Cell-derived Thyroid Cancer: Development of a Classification and Prognosis Prediction Model	COMPLETED	
NCT05197504	Predictive Biomarkers in Patients With Advanced Hepatocellular Carcinoma Treated With Systemic Therapy	COMPLETED	DRUG: atezolizumab plus bevacizumab
NCT04871321	Biomarker Discovery in Patients With Advanced Biliary Tract Cancer	COMPLETED	DRUG: nab-paclitaxel plus gemcitabine-cisplatin
NCT06573424	Tirellizumab + Anlotinib VS Anlotinib for MSS-type CRC	COMPLETED	COMBINATION_PRODUCT: Tislelizumab + anlotinib|DRUG: anlotinib
NCT05417451	Multi-Omics Study of the Effect and Mechanisms of Acupuncture on Psychoneurological Symptoms Among Breast Cancer Survivors	COMPLETED	OTHER: Acupuncture
NCT05729906	Dynamic Predictions of the Links Between Psychological and Physical Health of Older Patients in Nursing Home	COMPLETED	OTHER: psychological and physical tests
NCT07102069	Pharmacogenomic and Pharmacoepigenomic Studies of Antipsychotic Drugs in First-Episode Schizophrenia	COMPLETED	
NCT06759467	Diagnosis of Peritoneal Exfoliative Cytology-positive Gastric Cancer Based on Artificial Intelligence-driven Virtual Biopsy Technology	COMPLETED	DIAGNOSTIC_TEST: AI-Driven Virtual Biopsy for Diagnosis of Peritoneal Exfoliative Cytology-Positive Gastric Cance

of pre-analytical workflows, lack of CLIA-validated protocols, dependency on advanced computational infrastructure, challenges in reimbursement, and the absence of sufficiently powered, multi-center, clinically annotated cohorts for robust validation. Together, these limitations highlight the urgent need for simplified, cost-effective, and clinically deployable multi-omics workflows to enable the broader translation of these technologies into routine oncology practice.

Artificial intelligence (AI)-based biomarker discovery

Artificial intelligence plays a dual role in biomarker science enhancing multi-omics biomarker discovery and supporting clinical diagnostics through automated interpretation. AI- based biomarker discovery has emerged as a powerful approach for identifying clinically relevant molecular signatures from high-dimensional genomic and transcriptomic datasets. Traditional biomarker discovery relies largely on differential expression and hypothesis-driven analyses, which often fail to capture non-linear relationships, population-level heterogeneity, or complex regulatory interactions.

In contrast, AI and machine learning algorithms can simultaneously evaluate thousands of features, integrate multi-omics layers, and identify robust biomarkers that are predictive of disease progression, prognosis, and treatment response. Methods such as random forest, LASSO, gradient boosting, autoencoders, and graph-based deep learning models enable unbiased feature selection and can uncover hidden patterns that may remain undetected using standard statistical approaches. When combined with survival modeling and multi-cohort validation, AI-driven frameworks enhance biomarker reproducibility and translational potential, making them particularly valuable for rare and heterogeneous malignancies such as gallbladder cancer.

It is important to differentiate between AI models developed for biomarker discovery and those that are implemented in clinical practice. AI discovery models extract molecular signatures from omics or imaging data, whereas clinically approved AI tools primarily support diagnostic image interpretation and do not directly generate molecular biomarkers (Table 4).

AI and bioinformatics are effectively enabling to uncover genomic and proteomic biomarkers by swiftly analyzing big and complex data. A Random Survival Forest model including clinical and CT-based radiomic characteristics outperformed the conventional Cox model (0.775) in non-small cell lung cancer (NSCLC) with a C-index of 0.841 [66]. A DeepSurv model that combined radiomic and clinical data produced C-index values of 0.74–0.75 and AUCs of 0.73–0.76 at 8, 12, and 24 months [67]. An interpretable XGBoost model that included tumor and normal-lung radiomics produced a C-index of 0.76 on external validation in patients with locally advanced lung cancer treated with radiation [68]. In gastric cancer, a deep-learning radiogenomic model combining contrast-enhanced CT radiomics with clinical data predicted MSI status with an AUC of 0.883 in training and 0.802 in validation, suggesting that it can serve as a non-invasive "virtual biopsy" method [69]. Despite the high predictive accuracy of these AI models, challenges like low interpretability, overfitting risk, and a lack of prospective multi-center validation still exist.

Table 4 Clinically available AI-based biomarker products

S. No.	Product Name	Biomarker Type	Disease Area	Clinical Purpose & Status	Discovery Approach	Reference
1	**Galleri™ (GRAIL MCED Test)**	cfDNA methylation deep-learning classifier	Multi-cancer early detection	Detects > 50 cancers; predicts tissue of origin, **Laboratory Developed Test (LDT)**	Deep neural networks trained on > 15,000 cfDNA methylation profiles from CCGA study	[53]
2	**IDx-DR®(Digital Diagnostics)**	AI deep-learning retinal image classifier	Diabetic retinopathy	Assists in detecting prostate adenocarcinoma on whole-slide images, **FDA-cleared autonomous AI diagnosis**	CNN trained on > 900,000 expert-labeled fundus images	[58]
3	**Paige Prostate®**	Deep-learning histology cancer detector	Prostate cancer	AI detection of prostate carcinoma on whole-slide imaging, **Research-only**	Weakly supervised CNN trained on > 44,000 WSIs	[59]
4	**Ibex Galen™ AI**	CNN-based AI pathology biomarker	Breast & prostate cancer	Automated cancer detection & grading, **CE-IVDR marked)**	CNN trained on thousands of annotated pathology slides	[60]
5	**CNS Tumor Classifier (DKFZ)**	DNA methylation **Random Forest AI classifier**	Brain tumors	Molecular diagnosis & subtype classification, **Research-stage**	Random forest model trained on 2,801 methylation profiles	[61]
6	**DeepGlioma™**	Deep-learning molecular classifier	Glioma	Rapid intraoperative molecular diagnosis, **Research-stage**	Deep neural networks on spectroscopy + sequencing	[62]
7	**HRDetect**	AI-based mutational signature model (LASSO ML classifier)	Breast cancer	Identifies BRCA1/2 deficiency & HRD, **Research-stage**	LASSO logistic regression on 3,479 genome-wide mutational features	[63]
8	**PathAI®(Research-use AI)**	Deep-learning histopathology predictor	NSCLC	Predicts histologic subtype & driver mutations, **Research-stage**	CNN trained on > 4,000 H&E slides	[64]
9	**Melanoma Immune Response AI Model**	ML-based transcriptomic immune classifier	Melanoma	Predicts response to immunotherapy, **Research-stage**	ML trained on RNA-seq + mutation data for immune-score extraction	[65]

Role of bioinformatics and open-access data in biomarker discovery

Bioinformatics has been instrumental in managing and analyzing the vast datasets generated by genomic and proteomic studies. Computational tools enable pattern recognition, data integration, and predictive modeling, accelerating biomarker discovery. For instance, machine learning algorithms analyze high-dimensional omics data to identify cancer-specific signatures, such as gene expression profiles in breast cancer predicting recurrence [18]. Deep learning has enhanced histopathological image analysis, identifying spatial patterns linked to tumor aggressiveness, complementing molecular biomarkers [43]. Bioinformatics platforms like Bioconductor and Galaxy provide open-source tools for differential gene expression analysis, protein quantification, and pathway enrichment, democratizing access to advanced analytics [70]. These platforms provide defined settings for preprocessing, standardizing, and annotating high-dimensional omics data, which may then be effortlessly integrated into ML models for biomarker identification. For example, Bioconductor tools like as caret and mlr enable users to develop classification models on processed gene-expression datasets, whereas Galaxy provides automated pipelines that integrate feature selection, clustering, and predictive modeling [70].

Open-access data repositories have transformed biomarker discovery by enabling global data sharing and validation. The TCGA, launched in 2006, provides genomic, transcriptomic, and proteomic data for over 33 cancer types, facilitating the identification of novel biomarkers like IDH mutations in glioma [36]. The CPTAC integrates proteomic and genomic data, revealing biomarkers like MCT1 in lung adenocarcinoma [30]. cBioPortal offers user-friendly access to TCGA and other datasets, enabling researchers to explore genetic alterations and their clinical implications [71]. The Human Protein Atlas provides proteomic data on protein expression across tissues, aiding biomarker validation [72]. These repositories have reduced duplication, accelerated hypothesis testing, and fostered collaboration, particularly for rare cancers with limited cohorts.

A total of 26 clinical trials that were AI–based biomarkers or computational decision-support tools, found to have reached full completion, demonstrating that AI-driven tools are increasingly being evaluated in real-world clinical research settings (Table 5). These trials span diagnostics, prognostication, treatment-response prediction, surgical planning, imaging biomarkers, and digital pathology, reflecting the broad applicability of AI in translational oncology. In addition to these completed trials, the dataset also contained 41 studies that were actively recruiting, demonstrating a rapidly expanding pipeline of AI-assisted clinical research. These ongoing trials focus on next-generation applications such as multi-analyte AI blood tests, advanced radiogenomic signatures, AI-enabled clinical trial matching, automated surgical planning, early cancer detection tools, and immune-response prediction algorithms. The large number of recruiting studies underscores significant global interest and investment in the clinical deployment of AI-based biomarker technologies.

In addition, AI-based biomarker discovery pipelines are vulnerable to biases arising from underrepresentation of specific ethnic or geographic populations in training datasets. Such biases can lead to reduced diagnostic accuracy and unequal clinical performance. To make results fairer and more reliable, researchers now combine data from diverse populations and use methods that check for and correct these biases. Testing models on different groups and including information from large, international datasets helps make sure any new biomarkers discovered work well for everyone.

Bioinformatics and open-access data have also addressed tumor heterogeneity by enabling single-cell omics analysis, revealing subpopulations driving resistance [73]. Multi-omics integration, supported by bioinformatics, uncovers complex interactions between genomic and proteomic alterations, as seen in ovarian cancer studies identifying diagnostic panels [74]. However, challenges remain, including data standardization, privacy concerns, and computational demands, necessitating robust bioinformatics infrastructure.

Although AI has transformed biomarker discovery research, the clinical implementation of AI-based biomarkers remains limited. Most radiomic, radiogenomic, and deep-survival models described in the literature-including those for NSCLC, gastric cancer, and lung radiotherapy-represent research-stage tools that have not undergone regulatory validation or multicenter harmonization. These models perform well in retrospective cohorts but are vulnerable to dataset bias, overfitting, limited ethnic diversity, and lack of external validation, which restricts their diagnostic deployment.

In contrast, only a small number of AI tools have achieved FDA clearance or CE marking, and these predominantly address diagnostic image analysis rather than molecular biomarker discovery. The IDx-DR system for diabetic retinopathy screening and digital pathology algorithms such as Paige Prostate and Ibex Galen, which support histopathological detection and grading. Importantly, these systems do not replace pathologists but enhance detection consistency, reduce oversight errors, and serve as decision-support tools.

A clear gap therefore exists between AI models used to discover biomarkers (transcriptomic feature selection, mutational classifiers, immune-score prediction) and AI tools used clinically. Translational barriers include the

Table 5 List of clinical trials studies associated with AI-based biomarkers

NCT Number	Study Title	Study Status	Interventions
NCT06759467	Diagnosis of Peritoneal Exfoliative Cytology-positive Gastric Cancer Based on Artificial Intelligence-driven Virtual Biopsy Technology	COMPLETED	DIAGNOSTIC_TEST: AI-Driven Virtual Biopsy for Diagnosis of Peritoneal Exfoliative Cytology-Positive Gastric Cance
NCT06888089	Deep Clinical Trajectory Modeling to Optimize Accrual to Cancer Clinical Trials	COMPLETED	OTHER: AI-assisted MatchMiner Platform
NCT03955627	REJOIN Trial for Older Breast Cancer Survivors	COMPLETED	BEHAVIORAL: Relieving Joint Pain and Improving AI Adherence in Older Breast Cancer Survivors (REJOIN)
NCT05396807	REVERT - taRgeted thErapy for adVanced colorEctal canceR paTients	COMPLETED	DEVICE: AI
NCT07049627	AI-Based Prediction of Pathological Response in Rectal Cancer Patients Receiving Total Neoadjuvant Therapy	COMPLETED	OTHER: Total Neoadjuvant Therapy (TNT)
NCT06526754	Feasibility Analysis of LCD-SLA 3D Printing Technology for Overall Surgical Planning of Liver Malignant Tumors	COMPLETED	DEVICE: 3D-Printed Liver Model|PROCEDURE: Digital Simulation-Based Surgical Planning
NCT01564368	DWI in Assessing Treatment Response in Patients With Breast Cancer Receiving Neoadjuvant Chemotherapy	COMPLETED	PROCEDURE: diffusion-weighted magnetic resonance imaging
NCT06648512	Association of Ex Vivo Drug Response (EVDR) and Clinical Outcome in Acute Myeloid Leukaemia (EXCYTE-2)	COMPLETED	OTHER: No Interventions
NCT03688906	AI-EMERGE: Development and Validation of a Multi-analyte, Blood-based Colorectal Cancer Screening Test	COMPLETED	
NCT01322802	Vaccine Therapy in Treating Patients With Stage III-IV or Recurrent Ovarian Cancer	COMPLETED	BIOLOGICAL: pUMVC3-hIGFBP-2 multi-epitope plasmid DNA vaccine|OTHER: laboratory biomarker analysis
NCT01928186	FLT PET in Measuring Treatment Response in Patients With Newly Diagnosed Estrogen Receptor-Positive, HER2-Negative Stage I-III Breast Cancer	COMPLETED	DRUG: Fluorothymidine F-18|PROCEDURE: Positron Emission Tomography|OTHER: Laboratory Biomarker Analysis|DRUG: Run-in (short pre-surgery course) of endocrine-targeted therapy
NCT02737475	An Investigational Immuno-Therapy Study of Experimental Medication BMS-986,178 by Itself or in Combination With Nivolumab and/or Ipilimumab in Participants With Solid Cancers That Are Advanced or Have Spread	COMPLETED	DRUG: BMS-986,178|DRUG: Nivolumab|DRUG: Ipilimumab|BIOLOGICAL: Tetanus vaccine|BIOLOGICAL: DPV-001 vaccine|DRUG: Cyclophosphamide
NCT02206984	Endocrine Response in Women With Invasive Lobular Breast Cancer	COMPLETED	DRUG: Tamoxifen|DRUG: Anastrozole|DRUG: Fulvestrant
NCT01478477	Omega-3 Fatty Acids in Preventing Joint Symptoms in Patients With Stage I-III Breast Cancer Receiving Anastrozole, Exemestane, or Letrozole	COMPLETED	DIETARY_SUPPLEMENT: omega-3 fatty acid supplement|OTHER: Placebo|OTHER: Clinical assessments|OTHER: Assessment of therapy complications|PROCEDURE: Magnetic Resonance Imaging|PROCEDURE: Correlative/special studies
NCT02448420	Study of Palbociclib and Trastuzumab With Endocrine Therapy in HER2-positive Metastatic Breast Cancer	COMPLETED	DRUG: Palbociclib|DRUG: Trastuzumab|DRUG: Endocrine therapy|DRUG: Chemotherapy|DRUG: Antibody-Drug Conjugates
NCT05369156	The Effects of Chiropractic Care in Adults With Subclinical Spinal Pain	COMPLETED	OTHER: Chiropractic Care|OTHER: Control Group
NCT02730546	Pembrolizumab, Combination Chemotherapy, and Radiation Therapy Before Surgery in Treating Adult Patients With Locally Advanced Gastroesophageal Junction or Gastric Cardia Cancer That Can Be Removed by Surgery	COMPLETED	DRUG: Carboplatin|PROCEDURE: Computed Tomography|DRUG: Fluorouracil|OTHER: Laboratory Biomarker Analysis|DRUG: Leucovorin Calcium|DRUG: Oxaliplatin|DRUG: Paclitaxel|BIOLOGICAL: Pembrolizumab|PROCEDURE: Positron Emission Tomography|RADIATION: Radiation Therapy|PROCEDURE: Therapeutic Conventional Surgery
NCT04164069	Dasatinib for the Prevention of Oxaliplatin-Induced Neuropathy in Patients With Metastatic Gastrointestinal Cancer Receiving FOLFOX Chemotherapy With or Without Bevacizumab	COMPLETED	BIOLOGICAL: Bevacizumab|DRUG: Dasatinib|DRUG: Fluorouracil|DRUG: Leucovorin|DRUG: Leucovorin Calcium|DRUG: Oxaliplatin|OTHER: Quality-of-Life Assessment
NCT02833350	Safety and Efficacy Study of GDC-0853 Compared With Placebo and Adalimumab in Participants With Rheumatoid Arthritis (RA)	COMPLETED	DRUG: GDC-0853|DRUG: Adalimumab|DRUG: Folic Acid|DRUG: MTX|DRUG: Placebo
NCT02983227	A Study to Evaluate the Long-Term Safety and Efficacy of GDC-0853 in Participants With Moderate to Severe Rheumatoid Arthritis Enrolled in Study GA29350	COMPLETED	DRUG: GDC-0853

Table 6 Global comparison

S. No.	Platform	Strengths	Limitations
1.	NSG	Broad mutation detection	Cost, bioinformatics complexity, VUS issues
2.	MS Proteomics	PTM profiling, pathway insights	Reproducibility, dynamic range issues
3.	Liquid Biopsy	Non-invasive, longitudinal	Low ctDNA in early tumors, CHIP interference
4.	AI	Pattern recognition	Bias, overfitting, limited multi-ethnic data

need for prospective trials, explainability requirements, uncertainty quantification, regulatory validation pathways, and challenges integrating AI into existing laboratory information systems. These limitations underscore that AI-based biomarker identification is a promising but still evolving field whose real-world deployment is emerging only gradually. It is important to distinguish between AI models used for biomarker discovery and AI tools that are clinically deployed. While the former extract molecular signatures from omics data, the latter such as IDx-DR, Paige Prostate, and Ibex Galen support diagnostic decision-making but do not directly generate multi-omics biomarkers. This distinction is critical for interpreting their clinical applicability. Therefore, while AI has revolutionized biomarker discovery, its integration into routine molecular diagnostics is still emerging and requires multi-center validation, transparency in model interpretability, and standardized evaluation frameworks.

Impact on cancer diagnosis and prognostication

Diagnosis

Biomarkers have improved diagnostic accuracy by distinguishing malignant from benign lesions and identifying subtypes. HER-2 amplification, detected by fluorescence in situ hybridization or immunohistochemistry, guides anti-HER2 therapy in breast and gastric cancers [75]. PSA testing, combined with multiparametric MRI, enhances prostate cancer diagnosis [76]. Liquid biopsies detect early cancer-specific alterations, such as hypermethylated cfDNA in cancer or ncRNA [77, 78]. Multi-omics panels, leveraging bioinformatics, offer high sensitivity for early-stage cancers, as shown in ovarian cancer [74].

Prognostication

Biomarkers predict recurrence, treatment response, and survival. Oncotype DX and MammaPrint stratify breast cancer patients by recurrence risk, reducing unnecessary chemotherapy [17, 18]. KRAS mutations in colorectal cancer, present in 30–40% of cases, predict anti-EGFR therapy resistance [79]. Proteomic biomarkers like class III β-tubulin in ovarian cancer predict survival [31]. The RAF-MEK-ERK pathway, altered in half of cancers, is prognostic in breast cancer, with BRAF mutations linked to worse survival [80]. Liquid biopsies monitor minimal residual disease, detecting early recurrence in NSCLC [81].

Comparative assessment of multi-omics platforms

The Table 6 below address a new comparative summary.

Biomarker implementation in LMICs - opportunities and practical considerations

The adoption of genomic, proteomic, and multi-omics biomarkers in LMICs is limited by systemic barriers, including high equipment and consumable costs, lack of molecular pathology expertise, absence of reimbursement mechanisms, inconsistent electricity and cold-chain infrastructure, and limited access to high-performance computing [82, 83]. These constraints restrict deployment of NGS, MS-based proteomics, and liquid biopsy assays in routine oncology practice. The absence of reimbursement mechanisms for molecular testing and limited integration of precision oncology into national cancer control strategies further hinder adoption [84]. Within this setting, biomarker deployment must prioritize appropriate, scalable, and cost-effective technologies.

Several LMIC-adapted solutions have demonstrated feasibility. Targeted sequencing panels of 25–50 genes offer clinically relevant substantially lower cost than whole-exome or whole-genome assays and have been validated in resource-constrained settings [85] Low-cost methylation assays, including methylation-sensitive restriction enzyme (MSRE)–based qPCR, enable early cancer detection where array- or sequencing-based methylation profiling is impractical [86]. Portable nanopore sequencing platforms, such as the Oxford Nanopore MinION, allow near–real-time mutation detection without specialized infrastructure and have been deployed successfully in LMIC molecular diagnostic programs [87]. Cloud-based bioinformatics resources—including Galaxy, Terra, and DNAnexus—further circumvent the need for local high-performance computing, reducing hardware barriers to molecular interpretation [88].

At the system level, regional biobanking and sequencing hubs operating under shared-resource models can reduce duplication of costs and expand access to standardized molecular testing [89]. Telepathology and AI-assisted triage platforms have improved diagnostic turnaround times and mitigated shortages of pathology expertise in several LMICs [90]. Furthermore, pooled DNA sequencing strategies have emerged as a cost-saving approach for high-volume public hospitals conducting population-scale mutation screening [91]. Collectively, these context-appropriate approaches provide a practical roadmap for advancing biomarker-driven oncology in

LMICs and support more equitable global access to precision cancer care.

Policy-level recommendations for LMIC implementation

To accelerate equitable biomarker integration in LMICs, policy frameworks must prioritize (i) national cancer genomic programs with shared sequencing hubs, (ii) government-supported reimbursement for essential biomarker tests, (iii) international public–private partnerships for subsidized reagents and instruments, (iv) workforce development programs in molecular diagnostics and bioinformatics, and (v) harmonized quality-control standards for sample handling, NGS workflows, and data reporting. These measures ensure scalability, sustainability, and long-term integration of biomarker-driven oncology in resource-constrained settings. Strategic investment in scalable technologies, cloud-based computation, and regional resource-sharing models can enable LMICs to leapfrog traditional infrastructure constraints and rapidly adopt biomarker-driven precision oncology.

Challenges and future directions

Although multi-omics technologies have transformed biomarker discovery, still there are lot of challenges that need to be resolved. Challenges include tumor heterogeneity, biological variability. NGS provides high-resolution detection of somatic mutations and gene fusions but is limited by sequencing costs, bioinformatics complexity, and challenges in interpreting variants of uncertain significance [92]. Although, targeted NGS panels and focused proteomic assays provide cost-effective alternatives to whole-genome or deep proteomic profiling. Mass spectrometry enables deep protein and PTM profiling but suffers from batch effects, limited sensitivity for low-abundance proteins, and reproducibility issues across laboratories. Integrating these platforms introduces additional challenges, including multi-layer data harmonization, analytical noise, and computational demands.

Bioinformatics faces issues with data standardization and computational demands. Open-access repositories require improved interoperability and privacy safeguards. Cloud-based bioinformatics pipelines lower computational barriers by enabling remote analysis without local servers. Establishing regional testing hubs and biobanks can support multi-institutional sample processing and validation at scale. Moreover, open-access datasets enable researchers in LMICs to contribute to biomarker discovery without incurring high experimental costs. Public–private partnerships, government-supported screening initiatives, and capacity-building programs can further facilitate the integration of genomics and proteomics into cancer care in resource-limited settings.

A challenge in biomarker research is ensuring reproducible results, which is difficult due to differences in data collection, processing, and reporting between studies. To address these concerns, numerous international guidelines have been developed to aid with data standardization. MIAME (Minimum Information About a Microarray Experiment) guidelines provide a standardized framework for describing experimental design, sample preparation, array protocols, and data processing processes in transcriptomic studies, allowing researchers to generate transparent and reproducible datasets. In proteomics, the HUPO Proteomics Standards Initiative (HUPO-PSI) provides standardized formats and reporting criteria for mass spectrometry processes, protein identification, and quantification.

There are additional factors that influence the real-world implementation of these biomarkers, including cost-effectiveness, regulatory hurdles, and challenges in integrating them into clinical policy. Another concern is bringing a cancer biomarker test from research to clinical use, which necessitates significant validation and regulatory approval. Tests like Guardant360 CDx, FoundationOne Liquid CDx, and Oncotype DX demonstrate the level of evidence required to demonstrate a biomarker's accuracy, clinical utility, and safety prior to its adoption in standard healthcare. Future directions include standardizing protocols to enhance reproducibility, integrating multi-omics with AI for novel biomarkers, and advancing single-cell omics to address heterogeneity [73]. Despite cost and infrastructure constraints, LMICs can benefit substantially from emerging biomarker technologies through strategic adaptation.

Conclusion

Genomic and proteomic biomarker discovery, powered by bioinformatics and open-access data, has revolutionized cancer care. From CEA and PSA to NGS, MS, and liquid biopsies, scientific and technological progress has enhanced our understanding of cancer, improving diagnosis and prognostication.

Bioinformatics and repositories like TCGA and CPTAC have accelerated discovery by enabling data integration and collaboration. Despite challenges, multi-omics, AI, and global efforts promise to advance precision oncology, delivering personalized, effective care to patients worldwide.

Collectively, advances in multi-omics biomarker development, AI-assisted analysis, and scalable technologies provide a roadmap toward equitable precision oncology. Continued integration of omics data, machine learning, clinical validation, and health system reforms will be essential to narrow the global gap in cancer diagnosis and treatment.

Clinical trial number
Not applicable.

Authors' contributions
MR and RD wrote the manuscript. MR and RD prepared figures. MP reviewed and edited the manuscript. All authors reviewed the manuscript.

Funding
No funding.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
All authors agree that the work will be published in a journal and understand and agree to the full terms and conditions of its publication.

Competing interests
The authors declare no competing interests.

Received: 17 September 2025 / Accepted: 27 December 2025
Published online: 27 January 2026

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229–63. https://doi.org/10.3322/caac.21834 Epub 2024 Apr 4. PMID: 38572751.
2. Gold P, Freedman SO. Demonstration of tumor-specific antigens in human colonic carcinomata by immunological tolerance and absorption techniques. J Exp Med. 1965;121(3):439–62. https://doi.org/10.1084/jem.121.3.439. PMID: 14270243; PMCID: PMC2137957.
3. Schröder FH, Hugosson J, Roobol MJ, Tammela TL, Ciatto S, Nelen V, Kwiatkowski M, Lujan M, Lilja H, Zappa M, Denis LJ, Recker F, Berenguer A, Määttänen L, Bangma CH, Aus G, Villers A, Rebillard X, van der Kwast T, Blijenberg BG, Moss SM, de Koning HJ, Auvinen A. ERSPC Investigators. Screening and prostate-cancer mortality in a randomized European study. N Engl J Med. 2009;360(13):1320–8. https://doi.org/10.1056/NEJMoa0810084. Epub 2009 Mar 18. PMID: 19297566.
4. Lane DP, Crawford LV. T antigen is bound to a host protein in SV40-transformed cells. Nature. 1979;278(5701):261-3. https://doi.org/10.1038/278261a0. PMID: 218111.
5. Friend SH, Bernards R, Rogelj S, Weinberg RA, Rapaport JM, Albert DM, Dryja TP. A human DNA segment with properties of the gene that predisposes to retinoblastoma and osteosarcoma. Nature. 1986 Oct 16–22;323(6089):643-6. https://doi.org/10.1038/323643a0. PMID: 2877398.
6. Barbacid M. ras genes. Annu Rev Biochem. 1987;56:779–827. https://doi.org/10.1146/annurev.bi.56.070187.004023. PMID: 3304147.
7. Skoulidis F, Li BT, Dy GK, Price TJ, Falchook GS, Wolf J, Italiano A, Schuler M, Borghaei H, Barlesi F, Kato T, Curioni-Fontecedro A, Sacher A, Spira A, Ramalingam SS, Takahashi T, Besse B, Anderson A, Ang A, Tran Q, Mather O, Henary H, Ngarmchamnanrith G, Friberg G, Velcheti V, Govindan R. Sotorasib for lung cancers with *KRAS* p.G12C mutation. N Engl J Med. 2021;384(25):2371–81. https://doi.org/10.1056/NEJMoa2103695. Epub 2021 Jun 4. PMID: 34096690; PMCID: PMC9116274.
8. Miki Y, Swensen J, Shattuck-Eidens D, Futreal PA, Harshman K, Tavtigian S, Liu Q, Cochran C, Bennett LM, Ding W et al. A strong candidate for the breast and ovarian cancer susceptibility gene BRCA1. Science. 1994;266(5182):66–71. https://doi.org/10.1126/science.7545954. PMID: 7545954.
9. Wooster R, Bignell G, Lancaster J, Swift S, Seal S, Mangion J, Collins N, Gregory S, Gumbs C, Micklem G. Identification of the breast cancer susceptibility gene BRCA2. Nature. 1995 Dec 21–28;378(6559):789 – 92. https://doi.org/10.1038/378789a0. Erratum in: Nature 1996;379(6567):749. PMID: 8524414.
10. Schena M, Shalon D, Davis RW, Brown PO. Quantitative monitoring of gene expression patterns with a complementary DNA microarray. Science. 1995;270(5235):467 – 70. https://doi.org/10.1126/science.270.5235.467. PMID: 7569999.
11. Aebersold R, Mann M. Mass spectrometry-based proteomics. Nature. 2003;422(6928):198–207. https://doi.org/10.1038/nature01511. PMID: 12634793.
12. Lynch TJ, Bell DW, Sordella R, Gurubhagavatula S, Okimoto RA, Brannigan BW, Harris PL, Haserlat SM, Supko JG, Haluska FG, Louis DN, Christiani DC, Settleman J, Haber DA. Activating mutations in the epidermal growth factor receptor underlying responsiveness of non-small-cell lung cancer to gefitinib. N Engl J Med. 2004;350(21):2129–39. https://doi.org/10.1056/NEJMoa040938. Epub 2004 Apr 29. PMID: 15118073.
13. Flaherty KT, Puzanov I, Kim KB, Ribas A, McArthur GA, Sosman JA, O'Dwyer PJ, Lee RJ, Grippo JF, Nolop K, Chapman PB. Inhibition of mutated, activated BRAF in metastatic melanoma. N Engl J Med. 2010;363(9):809–19. https://doi.org/10.1056/NEJMoa1002011. PMID: 20818844; PMCID: PMC3724529.
14. Batta N, Pandey M. Mutational spectrum of tobacco associated oral squamous carcinoma and its therapeutic significance. World J Surg Oncol. 2019;17:1–2.
15. Dixit R, Pandey M, Shukla VK. Bioprospecting potential genetic biomarkers of gallbladder cancer. Mol Biol Rep. 2025;52(1):1–4.
16. Dixit R, Pandey M, Rajput M, Shukla VK. Unravelling of the comparative transcriptomic profile of gallbladder cancer using mRNA sequencing. Mol Biol Rep. 2022;49(7):6395–403.
17. Paik S, Shak S, Tang G, Kim C, Baker J, Cronin M, Baehner FL, Walker MG, Watson D, Park T, Hiller W, Fisher ER, Wickerham DL, Bryant J, Wolmark N. A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer. N Engl J Med. 2004;351(27):2817–26. https://doi.org/10.1056/NEJMoa041588. Epub 2004 Dec 10. PMID: 15591335.
18. van 't Veer LJ, Dai H, van de Vijver MJ, He YD, Hart AA, Mao M, Peterse HL, van der Kooy K, Marton MJ, Witteveen AT, Schreiber GJ, Kerkhoven RM, Roberts C, Linsley PS, Bernards R, Friend SH. Gene expression profiling predicts clinical outcome of breast cancer. Nature. 2002;415(6871):530-6. https://doi.org/10.1038/415530a. PMID: 11823860.
19. Parsons DW, Jones S, Zhang X, Lin JC, Leary RJ, Angenendt P, Mankoo P, Carter H, Siu IM, Gallia GL, Olivi A, McLendon R, Rasheed BA, Keir S, Nikolskaya T, Nikolsky Y, Busam DA, Tekleab H, Diaz LA Jr, Hartigan J, Smith DR, Strausberg RL, Marie SK, Shinjo SM, Yan H, Riggins GJ, Bigner DD, Karchin R, Papadopoulos N, Parmigiani G, Vogelstein B, Velculescu VE, Kinzler KW. An integrated genomic analysis of human glioblastoma multiforme. Science. 2008;321(5897):1807–12. https://doi.org/10.1126/science.1164382. Epub 2008 Sep 4. PMID: 18772396; PMCID: PMC2820389.
20. Mok TS, Wu Y-L, Ahn M-J, Garassino MC, Kim HR, Ramalingam SS, Shepherd FA, He Y, Akamatsu H, Theelen WS, Lee CK, Sebastian M, Templeton A, Mann H, Marotti M, Ghiorghiu S, Papadimitrakopoulou VA. AURA3 Investigators. Osimertinib or Platinum-Pemetrexed in EGFR T790M-Positive lung cancer. N Engl J Med. 2017;376(7):629–40. https://doi.org/10.1056/NEJMoa1612674. Epub 2016 Dec 6. PMID: 27959700; PMCID: PMC6762027.
21. FDA. (2020). FDA approves first liquid biopsy next-generation sequencing companion diagnostic test. FDA News Release. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-liquid-biopsy-next-generation-sequencing-companion-diagnostic-test [Accessed 10 Jul 2025].
22. Anderson NL, Anderson NG. The human plasma proteome: history, character, and diagnostic prospects. Mol Cell Proteomics. 2002;1(11):845 – 67. https://doi.org/10.1074/mcp.r200007-mcp200. Erratum in: Mol Cell Proteomics. 2003;2(1):50. PMID: 12488461.
23. Ong SE, Blagoev B, Kratchmarova I, Kristensen DB, Steen H, Pandey A, Mann M. Stable isotope labeling by amino acids in cell culture, SILAC, as a simple and accurate approach to expression proteomics. Mol Cell Proteomics. 2002;1(5):376 – 86. https://doi.org/10.1074/mcp.m200025-mcp200. PMID: 12118079.
24. Thompson A, Schäfer J, Kuhn K, Kienle S, Schwarz J, Schmidt G, Neumann T, Johnstone R, Mohammed AK, Hamon C. Tandem mass tags: a novel quantification strategy for comparative analysis of complex protein mixtures by MS/MS. Anal Chem. 2003;75(8):1895 – 904. https://doi.org/10.1021/ac026256O Erratum in: Anal Chem. 2003;75(18):4942. Johnstone, R . Erratum in: Anal Chem. 2006;78(12):4235. Mohammed, A Karim A. PMID: 12713048.
25. Gillet LC, Navarro P, Tate S, Röst H, Selevsek N, Reiter L, Bonner R, Aebersold R Targeted data extraction of the MS/MS spectra generated by data-independent acquisition: a new concept for consistent and accurate proteome

analysis. Mol Cell Proteom. 2012;11(6):O111016717. https://doi.org/10.1074/mcp.O111.016717. Epub 2012 Jan 18. PMID: 22261725; PMCID: PMC3433915.
26. Ueland FR, Desimone CP, Seamon LG, Miller RA, Goodrich S, Podzielinski I, Sokoll L, Smith A, van Nagell JR Jr, Zhang Z. Effectiveness of a multivariate index assay in the preoperative assessment of ovarian tumors. Obstet Gynecol. 2011;117(6):1289–97. https://doi.org/10.1097/AOG.0b013e31821b5118. PMID: 21606739.
27. Ludvigsen M, Thorlacius-Ussing L, Vorum H, Stender MT, Thorlacius-Ussing O, Honoré B. Proteomic characterization of colorectal cancer tissue from patients identifies novel putative protein biomarkers. Curr Issues Mol Biol. 2021;43(2):1043–56. https://doi.org/10.3390/cimb43020074. PMID: 34563043; PMCID: PMC8929084.
28. Pillai J, Chincholkar T, Dixit R, et al. A systematic review of proteomic biomarkers in oral squamous cell cancer. World J Surg Onc. 2021;19:315. https://doi.org/10.1186/s12957-021-02423-y.
29. Zhu Y, Zhu J, Lu C, Zhang Q, Xie W, Sun P, Dong X, Yue L, Sun Y, Yi X, Zhu T, Ruan G, Aebersold R, Huang S, Guo T. Identification of protein abundance changes in hepatocellular carcinoma tissues using PCT-SWATH. Proteom Clin Appl. 2019;13(1):e1700179. https://doi.org/10.1002/prca.201700179. Epub 2018 Nov 19. PMID: 30365225.
30. Gillette MA, Satpathy S, Cao S, Dhanasekaran SM, Vasaikar SV, Krug K, Petralia F, Li Y, Liang WW, Reva B, Krek A, Ji J, Song X, Liu W, Hong R, Yao L, Blumenberg L, Savage SR, Wendl MC, Wen B, Li K, Tang LC, MacMullan MA, Avanessian SC, Kane MH, Newton CJ, Cornwell M, Kothadia RB, Ma W, Yoo S, Mannan R, Vats P, Kumar-Sinha C, Kawaler EA, Omelchenko T, Colaprico A, Geffen Y, Maruvka YE, da Veiga Leprevost F, Wiznerowicz M, Gümüş ZH, Veluswamy RR, Hostetter G, Heiman DI, Wyczalkowski MA, Hiltke T, Mesri M, Kinsinger CR, Boja ES, Omenn GS, Chinnaiyan AM, Rodriguez H, Li QK, Jewell SD, Thiagarajan M, Getz G, Zhang B, Fenyö D, Ruggles KV, Cieslik MP, Robles AI, Clauser KR, Govindan R, Wang P, Nesvizhskii AI, Ding L, Mani DR, Carr SA. Clinical proteomic tumor analysis Consortium. Proteogenomic characterization reveals therapeutic vulnerabilities in lung adenocarcinoma. Cell. 2020;182(1):200–e22535. https://doi.org/10.1016/j.cell.2020.06.013. PMID: 32649874; PMCID: PMC7373300.
31. Roque DM, Buza N, Glasgow M, Bellone S, Bortolomai I, Gasparrini S, Cocco E, Ratner E, Silasi DA, Azodi M, Rutherford TJ, Schwartz PE, Santin AD. Class III β-tubulin overexpression within the tumor microenvironment is a prognostic biomarker for poor overall survival in ovarian cancer patients treated with neoadjuvant carboplatin/paclitaxel. Clin Exp Metastasis. 2014;31(1):101–10. Epub 2013 Sep 5. PMID: 24005572; PMCID: PMC3947146.
32. Pepe MS, Etzioni R, Feng Z, Potter JD, Thompson ML, Thornquist M, Winget M, Yasui Y. Phases of biomarker development for early detection of cancer. J Natl Cancer Inst. 2001;93(14):1054-61. https://doi.org/10.1093/jnci/93.14.1054. PMID: 11459866.
33. Mok TS, Wu YL, Thongprasert S, Yang CH, Chu DT, Saijo N, Sunpaweravong P, Han B, Margono B, Ichinose Y, Nishiwaki Y, Ohe Y, Yang JJ, Chewaskulyong B, Jiang H, Duffield EL, Watkins CL, Armour AA, Fukuoka M. Gefitinib or carboplatin-paclitaxel in pulmonary adenocarcinoma. N Engl J Med. 2009;361(10):947–57. https://doi.org/10.1056/NEJMoa0810699. Epub 2009 Aug 19. PMID: 19692680.
34. FDA. FDA authorizes first next generation sequencing-based test to detect very low levels of remaining cancer cells in patients with acute lymphoblastic leukemia or multiple myeloma. (2018). FDA News Release. https://www.fda.gov/news-events/press-announcements/fda-authorizes-first-next-generation-sequencing-based-test-detect-very-low-levels-remaining-cancer [Accessed 10 Jul 2025].
35. Druley TE, Vallania FL, Wegner DJ, Varley KE, Knowles OL, Bonds JA, Robison SW, Doniger SW, Hamvas A, Cole FS, Fay JC, Mitra RD. Quantification of rare allelic variants from pooled genomic DNA. Nat Methods. 2009;6(4):263–5. https://doi.org/10.1038/nmeth.1307. Epub 2009 Mar 1. PMID: 19252504; PMCID: PMC2776647.
36. Cancer Genome Atlas Research Network, Weinstein JN, Collisson EA, Mills GB, Shaw KR, Ozenberger BA, Ellrott K, Shmulevich I, Sander C, Stuart JM. The cancer genome atlas Pan-Cancer analysis project. Nat Genet. 2013;45(10):1113–20. https://doi.org/10.1038/ng.2764. PMID: 24071849; PMCID: PMC3919969.
37. Petricoin EF, Ardekani AM, Hitt BA, Levine PJ, Fusaro VA, Steinberg SM, Mills GB, Simone C, Fishman DA, Kohn EC, Liotta LA. Use of proteomic patterns in serum to identify ovarian cancer. Lancet. 2002;359(9306):572-7. https://doi.org/10.1016/S0140-6736(02)07746-2. PMID: 11867112.
38. Addona TA, Abbatiello SE, Schilling B, Skates SJ, Mani DR, Bunk DM, Spiegelman CH, Zimmerman LJ, Ham AJ, Keshishian H, Hall SC, Allen S, Blackman RK, Borchers CH, Buck C, Cardasis HL, Cusack MP, Dodder NG, Gibson BW, Held JM, Hiltke T, Jackson A, Johansen EB, Kinsinger CR, Li J, Mesri M, Neubert TA, Niles RK, Pulsipher TC, Ransohoff D, Rodriguez H, Rudnick PA, Smith D, Tabb DL, Tegeler TJ, Variyath AM, Vega-Montoto LJ, Wahlander A, Waldemarson S, Wang M, Whiteaker JR, Zhao L, Anderson NL, Fisher SJ, Liebler DC, Paulovich AG, Regnier FE, Tempst P, Carr SA. Multi-site assessment of the precision and reproducibility of multiple reaction monitoring-based measurements of proteins in plasma. Nat Biotechnol. 2009;27(7):633–41. https://doi.org/10.1038/nbt.1546. Epub 2009 Jun 28. Erratum in: Nat Biotechnol. 2009;27(9):864. PMID: 19561596; PMCID: PMC2855883.
39. Metzker ML. Sequencing technologies - the next generation. Nat Rev Genet. 2010;11(1):31–46. https://doi.org/10.1038/nrg2626. Epub 2009 Dec 8. PMID: 19997069.
40. Aebersold R, Mann M. Mass-spectrometric exploration of proteome structure and function. Nature. 2016;537(7620):347–55. https://doi.org/10.1038/nature19949. PMID: 27629641.
41. Wan JCM, Massie C, Garcia-Corbacho J, Mouliere F, Brenton JD, Caldas C, Pacey S, Baird R, Rosenfeld N. Liquid biopsies come of age: towards implementation of Circulating tumour DNA. Nat Rev Cancer. 2017;17(4):223–38. https://doi.org/10.1038/nrc.2017.7. Epub 2017 Feb 24. PMID: 28233803.
42. Drendel V, Heckelmann B, Schell C, et al. Proteomic distinction of renal Oncocytomas and chromophobe renal cell carcinomas. Clin Proteom. 2018;15:25. https://doi.org/10.1186/s12014-018-9200-6.
43. Esteva A, Kuprel B, Novoa RA, Ko J, Swetter SM, Blau HM, Thrun S. Dermatologist-level classification of skin cancer with deep neural networks. Nature. 2017;542(7639):115–118. https://doi.org/10.1038/nature21056. Epub 2017 Jan 25. Erratum in: Nature. 2017;546(7660):686. doi: 10.1038/nature22985. PMID: 28117445; PMCID: PMC8382232.
44. Cong L, Ran FA, Cox D, Lin S, Barretto R, Habib N, Hsu PD, Wu X, Jiang W, Marraffini LA, Zhang F. Multiplex genome engineering using CRISPR/Cas systems. Science. 2013;339(6121):819–23. https://doi.org/10.1126/science.1231143. Epub 2013 Jan 3. PMID: 23287718; PMCID: PMC3795411.
45. Paik S, Shak S, Tang G, van 't Veer LJ, Dai H, van de Vijver MJ, et al. A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer. N Engl J Med. 2004;351(27):2817–26.
46. Davies H, Glodzik D, Morganella S, et al. HRDetect is a predictor of BRCA1 and BRCA2 deficiency based on mutational signatures. Nat Med. 2017;23(4):517–25.
47. Lanman RB, Mortimer SA, Zill OA, et al. Analytical and clinical validation of a digital sequencing panel for detection of circulating tumor DNA. PLoS Med. 2015;12(10):e1001880.
48. Frampton GM, Fichtenholtz A, Otto GA, Wang K, Downing SR, He J, Schnall-Levin M, White J, Sanford EM, An P, Sun J, Juhn F, Brennan K, Iwanik K, Maillet A, Buell J, White E, Zhao M, Balasubramanian S, Terzic S, Richards T, Banning V, Garcia L, Mahoney K, Zwirko Z, Donahue A, Beltran H, Mosquera JM, Rubin MA, Dogan S, Hedvat CV, Berger MF, Pusztai L, Lechner M, Boshoff C, Jarosz M, Vietz C, Parker A, Miller VA, Ross JS, Curran J, Cronin MT, Stephens PJ, Lipson D, Yelensky R. Development and validation of a clinical cancer genomic profiling test based on massively parallel DNA sequencing. Nat Biotechnol. 2013;31(11):1023–31. https://doi.org/10.1038/nbt.2696. Epub 2013 Oct 20. PMID: 24142049; PMCID: PMC5710001.
49. Lanman RB, Mortimer SA, Zill OA, et al. Analytical and clinical validation of a digital sequencing panel for quantitative, highly accurate evaluation of cell-free Circulating tumor DNA. PLoS ONE. 2015;10(10):e0140712.
50. Carter P et al. Jan. Does molecular profiling of tumors using the Caris molecular intelligence platform improve outcomes for cancer patients? *Oncotarget* vol. 9,10 9456–9467. 16 2018, https://doi.org/10.18632/oncotarget.24258
51. Beaubier N, Tell R, Lau D. Clinical validation of the tempus xT next-generation targeted oncology sequencing assay. Oncotarget. 2019;10(24):2384–96.
52. Zehir A, Benayed R, Shah RH, Syed A, Middha S, Kim HR, Srinivasan P, Gao J, Chakravarty D, Devlin SM, Hellmann MD, Barron DA, Schram AM, Hameed M, Dogan S, Ross DS, Hechtman JF, DeLair DF, Yao J, Mandelker DL, Cheng DT, Chandramohan R, Mohanty AS, Ptashkin RN, Jayakumaran G, Prasad M, Syed MH, Rema AB, Liu ZY, Nafa K, Borsu L, Sadowska J, Casanova J, Bacares R, Kiecka IJ, Razumova A, Son JB, Stewart L, Baldi T, Mullaney KA, Al-Ahmadie H, Vakiani E, Abeshouse AA, Penson AV, Jonsson P, Camacho N, Chang MT, Won HH, Gross BE, Kundra R, Heins ZJ, Chen HW, Phillips S, Zhang H, Wang J, Ochoa A, Wills J, Eubank M, Thomas SB, Gardos SM, Reales DN, Galle J, Durany R, Cambria R, Abida W, Cercek A, Feldman DR, Gounder MM, Hakimi AA, Harding JJ, Iyer G, Janjigian YY, Jordan EJ, Kelly CM, Lowery MA, Morris LGT, Omuro AM, Raj N, Razavi P, Shoushtari AN, Shukla N, Soumerai TE, Varghese AM, Yaeger R, Coleman J, Bochner B, Riely GJ, Saltz LB, Scher HI, Sabbatini PJ, Robson ME, Klimstra DS, Taylor BS, Baselga J, Schultz N, Hyman DM, Arcila ME, Solit DB, Ladanyi M, Berger MF. Mutational landscape of metastatic cancer

revealed from prospective clinical sequencing of 10,000 patients. Nat Med. 2017;23(6):703–713. https://doi.org/10.1038/nm.4333. Epub 2017 May 8. Erratum in: Nat Med. 2017;23(8):1004. doi: 10.1038/nm0817-1004c. PMID: 28481359; PMCID: PMC5461196.
53. Liu MC, Oxnard GR, Klein EA, Swanton C, Seiden MV, CCGA Consortium. Sensitive and specific multi-cancer detection and localization using methylation signatures in cell-free DNA. Ann Oncol. 2020;31(6):745–59. https://doi.org/10.1016/j.annonc.2020.02.011. Epub 2020 Mar 30. PMID: 33506766; PMCID: PMC8274402.
54. Faham M, Zheng J, Moorhead M, Carlton VE, Stow P, Coustan-Smith E, Pui CH, Campana D. Deep-sequencing approach for minimal residual disease detection in acute lymphoblastic leukemia. Blood. 2012;120(26):5173–80. https://doi.org/10.1182/blood-2012-07-444042. Epub 2012 Oct 16. PMID: 23074282; PMCID: PMC3537310.
55. Ghani H, et al. GPSai: A clinically validated AI tool for tissue of origin prediction during routine tumor profiling. Cancer Res Commun Vol. 2025;5(9):1477–89. https://doi.org/10.1158/2767-9764.CRC-25-0171.
56. McKiernan J et al. A novel urine exosome gene expression assay to predict High-grade prostate cancer at initial biopsy. JAMA Oncol 2,7 (2016): 882–9. https://doi.org/10.1001/jamaoncol.2016.0097
57. StewardDL, Carty SE, Sippel RS, Yang SP, Sosa JA, Sipos JA, Figge JJ, Mandel S, Haugen BR, Burman KD, Baloch ZW, Lloyd RV, Seethala RR, Gooding WE, Chiosea SI, Gomes-Lima C, Ferris RL, Folek JM, Khawaja RA, Kundra P, Loh KS, Marshall CB, Mayson S, McCoy KL, Nga ME, Ngiam KY, Nikiforova MN, Poehls JL, Ringel MD, Yang H, Yip L, Nikiforov YE. Performance of a Multigene Genomic Classifier in Thyroid Nodules With Indeterminate Cytology: A Prospective Blinded Multicenter Study. JAMA Oncol. 2019;5(2):204–12. https://doi.org/10.1001/jamaoncol.2018.4616 Erratum in:JAMA Oncol. 2019 Feb 1;5(2):271. doi: 10.1001/jamaoncol.2018.6413. PMID: 30419129; PMCID: PMC6439562.
58. Abràmoff MD, Lavin PT, Birch M, Shah N, Folk JC. Pivotal trial of an autonomous AI-based diagnostic system for detection of diabetic retinopathy in primary care offices. NPJ Digit Med. 2018;1:39. https://doi.org/10.1038/s41746-018-0040-6. PMID: 31304320; PMCID: PMC6550188.
59. Campanella G, Hanna MG, Geneslaw L, Miraflor A, Werneck Krauss Silva V, Busam KJ, Brogi E, Reuter VE, Klimstra DS, Fuchs TJ. Clinical-grade computational pathology using weakly supervised deep learning on whole slide images. Nat Med. 2019;25(8):1301–9. https://doi.org/10.1038/s41591-019-0508-1. Epub 2019 Jul 15. PMID: 31308507; PMCID: PMC7418463.
60. Lami K, Yoon HS, Parwani AV, Pham HH, Tachibana Y, Linhart C, Grinwald M, Vecsler M, Fukuoka J. Validation of prostate and breast cancer detection artificial intelligence algorithms for accurate histopathological diagnosis and grading: a retrospective study with a Japanese cohort. Pathology. 2024;56(5):633–42.
61. Capper D, Jones DTW, Sill M, Nature., Capper D, Jones DTW, Sill M, Hovestadt V, Schrimpf D, Sturm D, Koelsche C, Sahm F, Chavez L, Reuss DE, Kratz A, Wefers AK, Huang K, Pajtler KW, Schweizer L, Stichel D, Olar A, Engel NW, Lindenberg K, Harter PN, Braczynski AK, Plate KH, Dohmen H, Garvalov BK, Coras R, Hölsken A, Hewer E, Bewerunge-Hudler M, Schick M, Fischer R, Beschorner R, Schittenhelm J, Staszewski O, Wani K, Varlet P, Pages M, Temming P, Lohmann D, Selt F, Witt H, Milde T, Witt O, Aronica E, Giangaspero F, Rushing E, Scheurlen W, Geisenberger C, Rodriguez FJ, Becker A, Preusser M, Haberler C, Bjerkvig R, Cryan J, Farrell M, Deckert M, Hench J, Frank S, Serrano J, Kannan K, Tsirigos A, Brück W, Hofer S, Brehmer S, Seiz-Rosenhagen M, Hänggi D, Hans V, Rozsnoki S, Hansford JR, Kohlhof P, Kristensen BW, Lechner M, Lopes B, Mawrin C, Ketter R, Kulozik A, Khatib Z, Heppner F, Koch A, Jouvet A, Keohane C, Mühleisen H, Mueller W, Pohl U, Prinz M, Benner A, Zapatka M, Gottardo NG, Driever PH, Kramm CM, Müller HL, Rutkowski S, von Hoff K, Frühwald MC, Gnekow A, Fleischhack G, Tippelt S, Calaminus G, Monoranu CM, Perry A, Jones C, Jacques TS, Radlwimmer B, Gessi M, Pietsch T, Schramm J, Schackert G, Westphal M, Reifenberger G, Wesseling P, Weller M, Collins VP, Blümcke I, Bendszus M, Debus J, Huang A, Jabado N, Northcott PA, Paulus W, Gajjar A, Robinson GW, Taylor MD, Jaunmuktane Z, Ryzhova M, Platten M, Unterberg A, Wick W, Karajannis MA, Mittelbronn M, Acker T, Hartmann C, Aldape K, Schüller U, Buslei R, Lichter P, Kool M, Herold-Mende C, Ellison DW, Hasselblatt M, Snuderl M, Brandner S, Korshunov A, von Deimling A, Pfister SM, et al. DNA methylation-based classification of central nervous system tumours. Nature. 2018;555(7697):469–74. https://doi.org/10.1038/nature26000 doi:10.1038/nature26000. Epub 2018 Mar 14. PMID: 29539639; PMCID: PMC6093218.
62. Hollon T, Jiang C, Chowdury A, et al. Artificial-intelligence-based molecular classification of diffuse gliomas using rapid, label-free optical imaging. Nat Med. 2023;29:828–32. https://doi.org/10.1038/s41591-023-02252-4.
63. Davies H, Glodzik D, Morganella S, Yates LR, Staaf J, Zou X, Ramakrishna M, Martin S, Boyault S, Sieuwerts AM, Simpson PT, King TA, Raine K, Eyfjord JE, Kong G, Borg Å, Birney E, Stunnenberg HG, van de Vijver MJ, Børresen-Dale AL, Martens JW, Span PN, Lakhani SR, Vincent-Salomon A, Sotiriou C, Tutt A, Thompson AM, Van Laere S, Richardson AL, Viari A, Campbell PJ, Stratton MR, Nik-Zainal S. HRDetect is a predictor of BRCA1 and BRCA2 deficiency based on mutational signatures. Nat Med. 2017;23(4):517–25. https://doi.org/10.1038/nm.4292. Epub 2017 Mar 13. PMID: 28288110; PMCID: PMC5833945.
64. Coudray N, Ocampo PS, Sakellaropoulos T, Narula N, Snuderl M, Fenyö D, Moreira AL, Razavian N, Tsirigos A. Classification and mutation prediction from non-small cell lung cancer histopathology images using deep learning. Nat Med. 2018;24(10):1559–67. https://doi.org/10.1038/s41591-018-0177-5. Epub 2018 Sep 17. PMID: 30224757; PMCID: PMC9847512.
65. Lauss M, Donia M, Harbst K, Andersen R, Mitra S, Rosengren F, Salim M, Vallon-Christersson J, Törngren T, Kvist A, Ringnér M, Svane IM, Jönsson G. Mutational and putative neoantigen load predict clinical benefit of adoptive T cell therapy in melanoma. Nat Commun. 2017;8(1):1738. https://doi.org/10.1038/s41467-017-01460-0. Erratum in: Nat Commun. 2020;11(1):1714. doi: 10.1038/s41467-020-15531-2. PMID: 29170503; PMCID: PMC5701046.
66. Koyama J, Morise M, Furukawa T, Oyama S, Matsuzawa R, Tanaka I, Wakahara K, Yokota H, Kimura T, Shiratori Y, Kondoh Y, Hashimoto N, Ishii M. Artificial intelligence-based personalized survival prediction using clinical and radiomics features in patients with advanced non-small cell lung cancer. BMC Cancer. 2024;24(1):1417. https://doi.org/10.1186/s12885-024-13190-w. PMID: 39558311; PMCID: PMC11572056.
67. Hou KY, Chen JR, Wang YC, Chiu MH, Lin SP, Mo YH, Peng SC, Lu CF. Radiomics-Based deep learning prediction of overall survival in Non-Small-Cell lung cancer using Contrast-Enhanced computed tomography. Cancers (Basel). 2022;14(15):3798. https://doi.org/10.3390/cancers14153798. PMID: 35954461; PMCID: PMC9367244.
68. Luo T, Yan M, Zhou M, Dekker A, Appelt AL, Ji Y, Zhu J, de Ruysscher D, Wee L, Zhao L, Zhang Z. Improved prognostication of overall survival after radiotherapy in lung cancer patients by an interpretable machine learning model integrating lung and tumor radiomics and clinical parameters. Radiol Med. 2025;130(1):96–109. https://doi.org/10.1007/s11547-024-01919-3. Epub 2024 Nov 14. PMID: 39542968.
69. Jiang Z, Xie W, Zhou X, Pan W, Jiang S, Zhang X, Zhang M, Zhang Z, Lu Y, Wang D. A virtual biopsy study of microsatellite instability in gastric cancer based on deep learning radiomics. Insights Imaging. 2023;14(1):104. https://doi.org/10.1186/s13244-023-01438-1. PMID: 37286810; PMCID: PMC10247640.
70. Huber W, Carey VJ, Gentleman R, Anders S, Carlson M, Carvalho BS, Bravo HC, Davis S, Gatto L, Girke T, Gottardo R, Hahne F, Hansen KD, Irizarry RA, Lawrence M, Love MI, MacDonald J, Obenchain V, Oleś AK, Pagès H, Reyes A, Shannon P, Smyth GK, Tenenbaum D, Waldron L, Morgan M. Orchestrating high-throughput genomic analysis with bioconductor. Nat Methods. 2015;12(2):115–21. https://doi.org/10.1038/nmeth.3252. PMID: 25633503; PMCID: PMC4509590.
71. Cerami E, Gao J, Dogrusoz U, Gross BE, Sumer SO, Aksoy BA, Jacobsen A, Byrne CJ, Heuer ML, Larsson E, Antipin Y, Reva B, Goldberg AP, Sander C, Schultz N. The cBio cancer genomics portal: an open platform for exploring multidimensional cancer genomics data. Cancer Discov. 2012;2(5):401-4. https://doi.org/10.1158/2159-8290.CD-12-0095. Erratum in: Cancer Discov. 2012;2(10):960. PMID: 22588877; PMCID: PMC3956037.
72. Uhlén M, Fagerberg L, Hallström BM, Lindskog C, Oksvold P, Mardinoglu A, Sivertsson Å, Kampf C, Sjöstedt E, Asplund A, Olsson I, Edlund K, Lundberg E, Navani S, Szigyarto CA, Odeberg J, Djureinovic D, Takanen JO, Hober S, Alm T, Edqvist PH, Berling H, Tegel H, Mulder J, Rockberg J, Nilsson P, Schwenk JM, Hamsten M, von Feilitzen K, Forsberg M, Persson L, Johansson F, Zwahlen M, von Heijne G, Nielsen J, Pontén F. Proteomics. Tissue-based map of the human proteome. Science. 2015;347(6220):1260419. https://doi.org/10.1126/science.1260419. PMID: 25613900.
73. Navin N, Hicks J. Future medical applications of single-cell sequencing in cancer. Genome Med. 2011;3(5):31. https://doi.org/10.1186/gm247. PMID: 21631906; PMCID: PMC3219072.
74. Zhang, Zheng M, Hu Y, Gou R, Wang J, Nie X, Li X, Liu Q, Liu J, Lin B et al. Integrated multi-omics analysis of genomics, epigenomics, and transcriptomics in ovarian carcinoma. Aging (Albany NY). 2019;11(12):4198–4215. https://doi.org/10.18632/aging.102047. PMID: 31257224; PMCID: PMC6629004.
75. Slamon DJ, Godolphin W, Jones LA et al. Studies of the HER-2/neu proto-oncogene in human breast and ovarian cancer. Science (New York, N.Y.). 1989;244(4905):707–712. https://doi.org/10.1126/science.2470152. PMID: 2470152.

76. Ahmed HU, El-Shater Bosaily A, Brown LC, Gabe R, Kaplan R, Parmar MK, Collaco-Moraes Y, Ward K, Hindley RG, Freeman A, Kirkham AP, Oldroyd R, Parker C, Emberton M, PROMIS study group. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. Lancet. 2017;389(10071):815–22. https://doi.org/10.1016/S0140-6736(16)32401-1. Epub 2017 Jan 20. PMID: 28110982.
77. Li L, Sun Y. Circulating tumor DNA methylation detection as biomarker and its application in tumor liquid biopsy: advances and challenges. MedComm (2020). 2024;5(11):e766. https://doi.org/10.1002/mco2.766. PMID: 39525954; PMCID: PMC11550092.
78. Das D, Singh P, Pal M, Pandey M, Dixit R. Global perspective on the genetic, epigenetic, and transcriptomic basis of gallbladder cancer. Crit Rev Oncol/Hematol. 2025;214:104830. https://doi.org/10.1016/j.critrevonc.2025.104830.
79. Karapetis CS, Khambata-Ford S, Jonker DJ, O'Callaghan CJ, Tu D, Tebbutt NC, Simes RJ, Chalchal H, Shapiro JD, Robitaille S, Price TJ, Shepherd L, Au HJ, Langer C, Moore MJ, Zalcberg JR. K-ras mutations and benefit from cetuximab in advanced colorectal cancer. N Engl J Med. 2008;359(17):1757-65. https://doi.org/10.1056/NEJMoa0804385. PMID: 18946061.
80. Davies H, Bignell GR, Cox C, Stephens P, Edkins S, Clegg S, Teague J, Woffendin H, Garnett MJ, Bottomley W, Davis N, Dicks E, Ewing R, Floyd Y, Gray K, Hall S, Hawes R, Hughes J, Kosmidou V, Menzies A, Mould C, Parker A, Stevens C, Watt S, Hooper S, Wilson R, Jayatilake H, Gusterson BA, Cooper C, Shipley J, Hargrave D, Pritchard-Jones K, Maitland N, Chenevix-Trench G, Riggins GJ, Bigner DD, Palmieri G, Cossu A, Flanagan A, Nicholson A, Ho JW, Leung SY, Yuen ST, Weber BL, Seigler HF, Darrow TL, Paterson H, Marais R, Marshall CJ, Wooster R, Stratton MR, Futreal PA. Mutations of the BRAF gene in human cancer. Nature. 2002;417(6892):949–54. https://doi.org/10.1038/nature00766. Epub 2002 Jun 9. PMID: 12068308.
81. Chaudhuri AA, Chabon JJ, Lovejoy AF, Newman AM, Stehr H, Azad TD, Khodadoust MS, Esfahani MS, Liu CL, Zhou L, Scherer F, Kurtz DM, Say C, Carter JN, Merriott DJ, Dudley JC, Binkley MS, Modlin L, Padda SK, Gensheimer MF, West RB, Shrager JB, Neal JW, Wakelee HA, Loo BW Jr, Alizadeh AA, Diehn M. Early detection of molecular residual disease in localized lung cancer by Circulating tumor DNA profiling. Cancer Discov. 2017;7(12):1394–403. https://doi.org/10.1158/2159-8290.CD-17-0716. Epub 2017 Sep 24. PMID: 28899864; PMCID: PMC5895851.
82. Farmer P, Frenk J, Knaul FM, et al. Expansion of cancer care and control in countries of low and middle income: a call to action. Lancet. 2010;376(9747):1186–93.
83. Sullivan R, Alatise OI, Anderson BO, et al. Global cancer surgery: delivering safe, affordable, and timely cancer surgery. Lancet Oncol. 2015;16(11):1193–224.
84. Fojo T, Mailankody S, Lo A. Unintended consequences of expensive cancer therapeutics-the pursuit of marginal indications and a me-too mentality that stifles innovation and creativity: the John Conley lecture. JAMA Otolaryngol Head Neck Surg. 2014;140(12):1225–36.
85. Rivera-Colón G, Chapman JS, White J, et al. Implementation of targeted next-generation sequencing panels in developing countries: opportunities and challenges. J Glob Oncol. 2017;3(3):256–63.
86. Koch A, Joosten SC, Feng Z, et al. Analysis of DNA methylation in cancer: location revisited. Nat Rev Clin Oncol. 2018;15(7):459–66.
87. Quick J, Loman NJ, Duraffour S, et al. Real-time, portable genome sequencing for Ebola surveillance. Nature. 2016;530(7589):228–32.
88. Afgan E, Baker D, Batut B, et al. The galaxy platform for accessible, reproducible and collaborative biomedical analyses: 2018 update. Nucleic Acids Res. 2018;46(W1):W537–44.
89. Lin D, Alpert A, Chen K. Establishing regional biobanks to advance genomic medicine: challenges and opportunities. Genome Med. 2020;12:51.
90. Williams BJ, DaCosta P, Goacher E, et al. A systematic review of the benefits and challenges of digital pathology and telepathology. J Clin Pathol. 2018;71(6):463–9.
91. Schmitt MW, Loeb LA, Salk JJ. The potential of DNA sequencing-based detection of low-frequency mutations in cancer. Genome Med. 2016;8:89.
92. Marusyk A, Almendro V, Polyak K. Intra-tumour heterogeneity: a looking glass for cancer? Nat Rev Cancer. 2012;12(5):323 – 34. https://doi.org/10.1038/nrc3261. PMID: 22513401.

Publisher's note