



Predictive Genetic Biomarkers of Chemotherapy Response in Common Cancers: Current Evidence and Perspectives for Targeted Therapies

Yasamin Fateme Saremi ^{1*}

¹ North Tehran Branch, Islamic Azad University, Tehran, Iran.

Corresponding Author's E-mail: yfsaremi@gmail.com

Abstract

Predictive genetic Biomarkers have assumed a central role to the evolution of precision oncology by enabling individualized cancer treatment and improving therapeutic outcomes. This review comprehensively summarizes the current landscape of genetic biomarkers used to predict chemotherapy response across major various solid tumors, such as those affecting the breast and colorectum, lung, and other common cancers. We discuss the molecular basis of chemotherapy sensitivity and resistance, highlighting key mechanisms such as DNA repair alterations, gene mutations, epigenetic modifications, and tumor heterogeneity. Furthermore, we present a structured classification of predictive biomarkers, ranging from germline and somatic variants to gene-expression signatures and multi-omics-based profiles. The clinical utility of biomarker-guided targeted therapies is also evaluated, emphasizing their role in optimizing treatment selection, minimizing toxicity, and enhancing survival outcomes. Despite significant advances in genomic technologies, challenges remain in biomarker validation, standardization, and clinical translation, especially in relation to tumor heterogeneity and real-world implementation. Emerging approaches such as liquid biopsy and AI-based technologies, and integrated multi-omics analysis are expected to further refine predictive accuracy and support dynamic treatment monitoring. Additionally, ongoing research in diverse solid tumors highlights the expanding applicability of biomarkers in immunotherapy and targeted therapy selection. Overall, This review emphasizes the profound impact of predictive genetic biomarkers in modern oncology and their critical role in advancing personalized cancer therapy.

Keywords: Predictive genetic biomarkers; Chemotherapy response; Precision oncology; Targeted therapy; Molecular profiling.

Introduction

Despite considerable progress in diagnostic and therapeutic approaches, cancer continues to represent a major global burden of morbidity and mortality. Traditional chemotherapy has long served as a cornerstone of cancer management; however,

significant interpatient variability in therapeutic response and treatment-related toxicity continues to limit its effectiveness. Recent developments in precision oncology have highlighted the importance of predictive genetic biomarkers in selecting patients who are most likely to benefit from



COPYRIGHTS

The Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to Cite this Article:

Y. F. Saremi." Predictive Genetic Biomarkers of Chemotherapy Response in Common Cancers: Current Evidence and Perspectives for Targeted Therapies", Advanced Therapies Journal .vol. 8, no. 28, pp. 9- 17, 2026.

targeted therapeutic regimens. Genetic alterations, including somatic mutations, germline variants, and gene-expression signatures, have demonstrated considerable potential for predicting chemotherapy sensitivity and resistance, thereby enabling more personalized treatment strategies and improved clinical outcomes (1, 41).

The rapid evolution of genomic technologies, particularly NGS-based sequencing and molecular characterization platforms, has accelerated the discovery and clinical application of predictive biomarkers across multiple cancer types. These biomarkers not only facilitate treatment selection but also contribute to reducing unnecessary toxicity and healthcare costs associated with ineffective therapies. Furthermore, emerging methods such as liquid biopsy, pharmacogenomics, and multi-omics integration are expanding the scope of biomarker-guided precision medicine. Despite these advances, challenges related to biomarker validation, tumor diversity and clinical implementation remain substantial barriers to widespread adoption. Consequently, comprehensive evaluation of predictive genetic biomarkers is essential for advancing individualized cancer therapy and optimizing chemotherapy response prediction (1, 42).

Genetic Biomarkers as Predictors of Chemotherapy Response

Genetic biomarkers have emerged as critical tools in modern oncology for predicting individual responses to chemotherapeutic agents and facilitating personalized treatment strategies. Variations in both germline and somatic genes can influence drug absorption, metabolism, transport, and cellular sensitivity, thereby affecting treatment efficacy and toxicity. Advances in pharmacogenomics have advanced the detection of genetic alterations linked to with resistance or sensitivity to commonly used anticancer drugs. Biomarkers such as gene genetic variants, including SNPs, copy-number variations, and epigenetic alterations provide valuable insights into tumor behavior and therapeutic outcomes. Bringing these findings molecular indicators into clinical practice has improved patient stratification and optimized drug selection. Furthermore, biomarker-guided chemotherapy can reduce unnecessary exposure to ineffective treatments and minimize adverse effects. As precision oncology advances, genetic biomarkers are becoming increasingly important for tailoring treatment decisions to the molecular characteristics of individual patients and tumors. (1, 2)

Several Studies have revealed that the predictive value of genetic biomarkers across several major cancer types, including breast cancer, colorectal, lung, and ovarian malignancies. Alterations in DNA repair genes, drug-metabolizing enzymes, mismatch

repair pathways, and regulatory microRNAs have have been linked to variable responses to platinum-containing agents, taxanes, fluoropyrimidines, and other cytotoxic agents. New findings additionally highlight the role of epigenetic biomarkers and gene-expression signatures in recognizing individuals most likely to benefit from certain chemotherapy regimens. Despite the progress achieved, several limitations remain. regarding biomarker validation, standardization and clinical integration implementation. Large-scale prospective scientific studies and multidimensional omics approaches are expected to improve the reliability and applicability of predictive biomarkers in routine oncology practice. Ultimately, the integration of genomic information with targeted these treatment approaches may contribute to greater therapeutic efficacy and improved clinical outcomes (3, 4).

Classification of Predictive Genetic Biomarkers

Predictive genetic biomarkers may be grouped into different categories according to their biological origin, molecular characteristics, and clinical applications. The most widely recognized groups include germline genetic variants, somatic mutations, gene-expression signatures, epigenetic alterations, and pharmacogenomic markers. Germline biomarkers are inherited genetic variations that influence drug metabolism, toxicity, and treatment outcomes, whereas somatic biomarkers arise within tumor cells and directly affect therapeutic sensitivity or resistance. In addition, gene-expression profiles provide valuable information regarding tumor behavior and response to specific chemotherapeutic agents. Epigenetic biomarkers, including DNA methylation patterns and histone modifications, further contribute to treatment stratification by regulating gene activity without altering DNA sequences. The classification of these biomarkers is essential for determining patients with the highest potential to benefit from individualized treatment strategies and for advancing precision oncology. Advances in next-generation, high-throughput sequencing approaches have significantly expanded the spectrum of clinically relevant predictive biomarkers available for cancer management (5, 6).

Another important classification approach categorizes predictive biomarkers according to their functional roles in therapeutic decision-making. Pharmacodynamic biomarkers reflect the biological effects of treatment on tumor cells, while pharmacokinetic biomarkers influence drug absorption, distribution, metabolism, and elimination. Molecular predictive biomarkers may also be classified as single-gene markers, multigene panels, or integrated multi-omics signatures that combine genomic, transcriptomic, and epigenomic

data. Clinically validated examples include RAS mutations in colorectal cancer, BRCA1/2 alterations in breast and ovarian cancers, and microsatellite instability status in multiple solid tumors. These biomarkers not only predict chemotherapy response but also facilitate the choice of individualized targeted therapies and immunotherapeutic approaches. As biomarker research progresses, comprehensive molecular characterization is likely to enhance treatment personalization and improve clinical outcomes across diverse cancer types (7, 8).

Molecular Basis of Chemotherapy Resistance and Sensitivity

The cellular response to chemotherapeutic agents is governed by a complex network of molecular mechanisms that determine either drug sensitivity or resistance. Chemotherapy sensitivity is often associated with efficient drug uptake, activation of apoptotic pathways, intact DNA damage responses, and susceptibility to oxidative stress. In contrast, resistance develops through genetic and epigenetic alterations that enable tumor cells to survive cytotoxic insults. Key mechanisms include enhanced ABC transporter-driven drug efflux and increased DNA repair capacity, dysregulation of apoptosis-related proteins, and alterations in cell-cycle checkpoints. Mutations affecting tumor suppressor genes and oncogenic signaling pathways further contribute to therapeutic failure. Tumor heterogeneity and clonal evolution also play significant roles in generating resistant cellular subpopulations during treatment. Understanding these molecular determinants is vital for determining predictive biomarkers and developing strategies to improve chemotherapy clinical efficacy and patient-related outcomes (9, 10).

Recent evidence has reinforced the significance of cellular plasticity, metabolic reprogramming, tumor stem cells and their complex interactions within the tumor microenvironment as critical drivers of chemotherapy resistance. Alterations in major intracellular signaling networks such as PI3K/AKT/mTOR, MAPK, Wnt/ β -catenin, and NF- κ B can promote survival and reduce drug-induced apoptosis. In addition, epigenetic modifications, non-coding RNAs, and transcriptional reprogramming contribute to adaptive resistance mechanisms that emerge during treatment. Conversely, tumors exhibiting defective DNA repair systems or impaired stress-response pathways often demonstrate increased sensitivity to DNA-damaging agents and other cytotoxic drugs. Advances in multi-omics technologies have improved the characterization of these molecular processes and facilitated the discovery of potential new therapeutic targets. Further investigation understanding of resistance and sensitivity mechanisms is expected

to support the the formulation of individualized therapeutic regimens approaches and enhance the effectiveness of precision oncology (11, 12).

Biomarkers in Breast Cancer

Breast cancer is a biologically diverse disease defined by diverse molecular subtypes, each showing different biological profiles and therapeutic responses. The identification of predictive biomarkers has have established themselves as an integral part of precision oncology, supporting the optimization of therapeutic approaches selection and improve patient outcomes. Established biomarkers estrogen receptor (ER), progesterone receptor (PR), and HER2 are commonly evaluated to guide systemic therapy and predict responsiveness to both chemotherapy and targeted treatments. In addition, genomic assays and gene-expression signatures have enhanced risk stratification and treatment decision-making in early-stage disease. Recent advances in molecular profiling have also revealed the significance of tumor-infiltrating lymphocytes, ctDNA and other promising biomarkers in predicting therapeutic efficacy. These biomarkers contribute to individualized treatment approaches by determining which patients are most likely to benefit from targeted interventions while avoiding unnecessary toxicity. Consequently, biomarker-guided management has have evolved into an integral part of modern breast cancer care and precision medicine (13, 14).

Beyond traditional molecular markers, extensive research has focused on identifying novel genetic and epigenetic predictors of chemotherapy response in breast cancer. Alterations in BRCA1 and BRCA2 genes, DNA repair pathways, immune-related signatures, and molecular subtyping profiles have demonstrated predictive value for sensitivity to platinum-based agents and other cytotoxic therapies. Furthermore, advances in advanced genomic sequencing and liquid biopsy-based methods technologies have facilitated the detection of dynamic biomarkers that reflect tumor evolution during treatment. Predictive biomarkers are especially important for triple-negative and HER2-positive breast cancer subtypes, where treatment responses can vary substantially among patients. Despite significant progress, challenges related to tumor heterogeneity, biomarker validation, and clinical implementation remain unresolved. Ongoing translational research and extensive prospective studies are expected to improve the combination of predictive adoption of biomarkers in routine clinical practice and further advance tailored treatment approaches in breast cancer (15, 16).

Biomarkers in Colorectal Cancer

CRC is one of the most frequently occurring cancer

types worldwide and exhibits considerable molecular heterogeneity that influences disease progression and therapeutic response. The identification of predictive biomarkers has become increasingly important to refine therapeutic strategies and achieve better clinical outcomes in patients with CRC. Molecular biomarkers such as mutations in RAS and BRAF, together with MSI, dMMR, and HER2 status amplification have shown strong potential for predicting responses to chemotherapy, targeted therapies, and immunotherapy. In addition to tissue-based markers, ctDNA and other cell-free DNA components nucleic acids, and microRNA profiles have emerged as promising biomarkers for non-invasive assessment of disease monitoring and therapeutic selection. Advances in genomic and transcriptomic technologies have facilitated the discovery of novel molecular signatures associated with therapeutic sensitivity and resistance. These innovations have contributed substantially to the implementation of precision medicine approaches in colorectal cancer management. Consequently, biomarker-driven therapeutic decision-making is increasingly recognized as a cornerstone of personalized CRC treatment (17, 18).

Recent research has expanded the spectrum of clinically relevant biomarkers beyond conventional genetic alterations to include epigenetic modifications, tumor mutational burden, immune-related signatures, and molecular subtypes. Predictive biomarkers represent a valuable tool a critical role in identifying patients who may derive greater benefit from anti-EGFR therapies, immune checkpoint inhibitors, and combination treatment regimens. For example, RAS mutational status remains a key determinant of clinical response to anti-EGFR-targeted antibodies, while MSI-high tumors exhibit enhanced responsiveness to immunotherapy. Furthermore, comprehensive molecular profiling has improved the understanding of resistance mechanisms and enabled the development of individualized treatment strategies. Despite these advances, challenges related to biomarker validation, standardization, and accessibility continue to limit widespread clinical implementation. Future studies integrating integrative omics approaches coupled with AI technologies -based analyses are may further improve predictive biomarker discovery and improve therapeutic outcomes in colorectal cancer patients (19, 20).

Biomarkers in Lung Cancer

Globally, lung cancer remains a major contributor to cancer-related mortality, with significant molecular heterogeneity influencing disease progression and therapeutic response. The characterization of predictive biomarkers has

transformed the management of lung cancer by enabling patient-specific therapeutic approaches and improving clinical outcomes. In non-small cell lung cancer (NSCLC), genomic alterations including mutations affecting EGFR, KRAS, and BRAF and rearrangements involving ALK, ROS1, RET, and NTRK, have been recognized as critical determinants of treatment selection and response prediction. In addition to genetic alterations, biomarkers including PD-L1 levels, tumor mutational burden, and circulating tumor DNA have demonstrated substantial clinical value in guiding targeted therapies and immunotherapeutic interventions. Technological advances in next-generation sequencing have facilitated comprehensive molecular profiling, allowing clinicians to identify actionable alterations and optimize therapeutic decision-making. As a result, biomarker-driven treatment has become a fundamental component of precision oncology in lung cancer management (21, 22).

Recent investigations have expanded the spectrum of predictive biomarkers beyond established genomic drivers to include epigenetic signatures, liquid biopsy markers, radiomic features, and multi-omics profiles. Emerging evidence suggests that circulating tumor cells (CTCs) and extracellular vesicles (EVs), and gene-expression signatures may provide valuable a better understanding of treatment response, disease monitoring, and resistance-related mechanisms. Furthermore, the application of AI and machine learning approaches approaches has accelerated biomarker discovery and improved the interpretation of complex molecular datasets. These innovations have enhanced the ability to predict chemotherapy sensitivity, identify resistance pathways, and monitor tumor evolution throughout treatment. Despite substantial progress, challenges related to biomarker standardization, clinical validation, and accessibility continue to limit widespread implementation. Future research focusing on integrated molecular profiling and real-time biomarker assessment is expected to further improve personalized therapeutic strategies and patient outcomes in lung cancer (23, 24).

Biomarkers in Other Common Solid Tumors

Beyond breast, colorectal, and lung cancers, a wide spectrum of other solid tumors including pancreatic, prostate, gastric, and ovarian cancers also exhibit complex molecular landscapes that can be exploited for predictive biomarker development. These tumors are characterized by substantial genetic heterogeneity, which significantly influences treatment response and clinical outcomes. Clinically used biomarkers such as CA-125 in ovarian cancer and PSA in prostate cancer, and CA19-9 in pancreatic cancer have long been used in clinical practice, although their predictive accuracy for chemotherapy response remains

limited. Recent advances in molecular oncology have shifted the focus toward genomic and transcriptomic biomarkers, such as BRCA1/2 mutations together with impaired homologous recombination repair, and mismatch repair deficiency, which provide more robust predictive value for targeted therapies and platinum-based chemotherapy. In addition, TMB and MSI are increasingly regarded as biomarkers relevant to a wide range of cancer types, with therapeutic implications across multiple solid tumor types. The integration of these molecular markers into clinical workflows has enhanced patient stratification and facilitated more individualized treatment approaches. However, variability in tumor biology and biomarker expression continues to pose challenges for standardization and clinical implementation (25, 26).

In addition to genomic alterations, Emerging research underscores the significance of circulating and microenvironment-derived biomarkers in other solid tumors. Liquid biopsy components including circulating tumor DNA (ctDNA), as well as circulating tumor cells (CTCs), and non-coding RNAs have demonstrated promising utility in early detection, treatment monitoring, and prediction of therapeutic resistance. Furthermore, immune-related biomarkers, including PD-L1 levels and tumor-infiltrating lymphocytes (TILs), are increasingly recognized for their role in guiding immunotherapy across diverse tumor types. Advances in multi-omics technologies and AI-driven analytical platforms have further improved the identification of novel predictive signatures in heterogeneous tumor populations. These innovations are particularly relevant for cancers with limited therapeutic options, where traditional biomarkers fail to capture the full spectrum of tumor behavior. Despite significant progress, challenges such as assay standardization, inter-tumoral variability, and limited prospective validation studies remain major barriers. Future research focusing on integrative biomarker panels is expected to enhance predictive accuracy and support precision oncology in these malignancies (27, 28).

Clinical Utility of Biomarker-Guided Targeted Therapies

The clinical utility of biomarker-guided targeted therapies has transformed modern oncology by enabling precise patient stratification and individualized therapeutic selection. Predictive biomarkers play a central contribution to identifying patients who are most likely to respond favorably to specific targeted agents, thereby increasing treatment efficacy and limiting unnecessary toxicity. In various solid tumors, genomic alterations such as EGFR alterations and ALK rearrangements, and HER2 amplification have become established indicators for the use of corresponding agents targeting tyrosine kinases and

monoclonal antibodies. Similarly, biomarkers such as PD-L1 levels and tumor mutational burden guide immunotherapy decisions across multiple cancer types. The integration of biomarker testing into standard clinical practice has led to considerable improvements in response rates and progression-free survival in selected patient populations. Moreover, companion diagnostic platforms and next-generation sequencing technologies have facilitated rapid and comprehensive molecular profiling. These advances collectively highlight the critical importance of biomarker-driven approaches in modern precision oncology practice (29, 30).

Despite substantial progress, multiple barriers limit the widespread clinical implementation of biomarker-guided targeted therapies. Variations in tumor heterogeneity across and within tumors frequently contribute to differences in biomarker expression, and inconsistent treatment responses. Additionally, resistance mechanisms frequently emerge through secondary mutations, pathway reactivation, or bypass signaling, reducing long-term treatment efficacy. Approaches based on liquid biopsy, such as circulating tumor DNA and circulating tumor cells, have gained recognition as promising tools for real-time monitoring of therapeutic response and resistance evolution. Furthermore, the use of integrated multi-omics data and artificial intelligence is enhancing the predictive accuracy of biomarker-based models. However, issues related to assay standardization, cost-effectiveness, and accessibility remain significant barriers to widespread clinical adoption. Continuing clinical trials and translational research efforts are expected to refine biomarker-guided strategies and expand their utility across diverse cancer types (31, 32).

Challenges in Clinical Implementation and Translational Research

Despite remarkable advances in identifying predictive genetic biomarkers and developing targeted therapies, their successful translation for widespread adoption in clinical practice remains limited by multiple interrelated challenges. One of the major barriers is the insufficient standardization in biomarker detection methods, including variability in assay platforms, sample processing, and interpretation of molecular data. In addition, tumor heterogeneity both spatial and temporal significantly complicates the reproducibility and reliability of biomarker-based predictions across patient populations. Many promising biomarkers fail to progress beyond early-phase studies due to insufficient validation in large, prospective, multi-center clinical trials. Furthermore, the gap between preclinical discoveries and clinical application remains wide, partly due to complex regulatory requirements

and limited integration between laboratory research and clinical oncology workflows. The absence of harmonized guidelines for biomarker qualification further delays clinical adoption and contributes to inconsistent implementation across healthcare systems. These limitations collectively restrict the full realization of precision oncology in everyday clinical practice (33, 34).

Another critical issue in translational research is the difficulty in demonstrating clear clinical utility and cost-effectiveness of biomarker-guided strategies in real-world settings. Although liquid biopsy, multi-omics profiling, and artificial intelligence-based models have shown great promise, their integration into routine care is still in early stages due to limited prospective validation and infrastructure constraints. Variability in healthcare resources, particularly between developed and developing regions, further exacerbates disparities in access to advanced molecular diagnostics. In addition, resistance mechanisms and tumor evolution over time reduce the long-term predictive accuracy of many currently available biomarkers. Ethical considerations, data sharing limitations, and regulatory uncertainties also pose significant obstacles to large-scale implementation. To overcome these challenges, future translational research must focus on robust clinical trial designs, standardized analytical pipelines, and interdisciplinary collaboration between researchers, clinicians, and regulatory agencies. Ultimately, translating scientific discoveries into clinical practice is essential for maximizing the impact of predictive biomarkers in precision oncology (35, 36).

Future Directions in Precision Oncology

Breast cancer is a highly heterogeneous malignancy with various molecular subtypes that significantly influence clinical prognosis and response to therapy. The identification of predictive biomarkers has established themselves as a key pillar of precision oncology, supporting individualized treatment strategies and improved clinical outcomes. Established molecular biomarkers such as estrogen receptor (ER), progesterone receptor (PR), and HER2 remain fundamental in guiding systemic therapy selection. In addition, genomic molecular assays such as Oncotype DX and MammaPrint have enhanced risk stratification in early-stage disease and reduced overtreatment. The rapid evolution of next-generation sequencing technologies has further enabled the discovery of novel genetic alterations associated with chemotherapy sensitivity and resistance. Circulating tumor DNA and liquid biopsy techniques approaches have also emerged as promising non-invasive tools for real-time disease monitoring. These developments collectively highlight the increasing importance of molecular

profiling in modern breast cancer management (37, 38).

Beyond traditional biomarkers, emerging evidence has emphasized the importance of immune-related signatures, tumor microenvironment characteristics, and epigenetic modifications in forecasting treatment response. Biomarkers such as BRCA1/2-associated alterations and impaired homologous recombination repair are particularly important in identifying patients potentially benefiting from platinum-based chemotherapy and PARP inhibitors. Furthermore, gene-expression profiling has improved the understanding of intrinsic tumor subtypes and their therapeutic vulnerabilities. Despite these advances, challenges remain in clinical validation, assay harmonization and integration into routine practice. Inter-patient and intra-tumoral heterogeneity further complicate biomarker interpretation and clinical decision-making. Ongoing translational research is focusing on multi-omics integration and artificial intelligence-based predictive models to improve accuracy and clinical utility. These innovations are expected to significantly advance personalized treatment strategies in breast cancer (39, 40).

Conclusions

The growing body of research supports the central role of predictive genetic biomarkers in transforming cancer management from a standardized approach to a more tailored and individualized therapeutic strategy. Across major cancer types such as breast, colorectal, lung, and other solid tumors, biomarker-guided decision-making has demonstrated clear clinical value in predicting chemotherapy response, optimizing targeted therapy selection, and improving patient outcomes. Advances in genomic technologies, including next-generation sequencing and liquid biopsy platforms, have significantly expanded the range of detectable biomarkers and enabled continuous monitoring of tumor evolution. Despite these advancements, variability in biomarker performance, tumor heterogeneity, and lack of inadequate standardization continues to impede universal clinical implementation. Moreover, the combination of multi-omics information with AI-driven approaches has shown promise but still requires robust validation in large-scale prospective studies. Collectively, current evidence highlights that predictive genetic biomarkers are indispensable tools in modern precision oncology, yet their full clinical potential remains partially unrealized.

Looking forward, the future of biomarker-guided advancing cancer therapy relies on the integration of comprehensive molecular profiling with adaptive clinical trial designs and translational research frameworks. Harmonization of laboratory methods, improved bioinformatics pipelines, and stronger collaboration between researchers, clinicians, and

Table 1. Selected preclinical and clinical studies investigating probiotic-based approaches in colorectal cancer.

No.	Study (Author & Year)	Biomarker Type	Clinical Relevance	Key Findings	Ref
1	Derouane et al., 2022	Gene expression (BRCA-related)	Chemotherapy response	Improved prediction of neoadjuvant response	37
2	Tarighati et al., 2023	ER/PR/HER2	Treatment selection	Strong predictive value for targeted therapy	38
3	Wang et al., 2023	Immune signatures	Immunotherapy response	Correlates with checkpoint inhibitor efficacy	39
4	van den Ende et al., 2023	Genomic profiling	TNBC therapy response	Identifies platinum-sensitive patients	40
5	Telli et al., 2021	HRD score	PARP inhibitor response	Predicts sensitivity in BRCA-like tumors	41
6	Schmid et al., 2020	Tumor infiltrating lymphocytes	Prognosis	Higher TILs associated with better survival	42
7	Turner et al., 2019	ctDNA	Disease monitoring	Early detection of relapse	43
8	Cortazar et al., 2019	Pathologic complete response markers	Neoadjuvant therapy	Predictor of long-term survival	44

regulatory agencies will be essential to overcome existing translational barriers. In addition, expanding equitable access to advanced diagnostic technologies across healthcare systems will be critical to reduce disparities in cancer care. The development of standardized biomarker panels and clinically validated predictive models is expected to enhance treatment accuracy and cost-effectiveness. Ultimately, continued progress in understanding tumor biology and therapeutic resistance mechanisms will further strengthen the role of predictive biomarkers in guiding targeted therapies. This evolution will pave the way toward truly personalized oncology, where treatment decisions are driven by precise molecular characterization rather than empirical approaches, leading to enhanced survival and overall quality of life in patients with cancer.

knowledgements

Not applicable.

Funding

No funding was received.

Competing Interest

The authors declare no competing interests

Ethics approval and consent

Not applicable

Consent to publish

Not applicable

References

- Carr DF, Turner RM, Pirmohamed M. Pharmacogenomics of anticancer drugs: Personalising the choice and dose to manage drug response. *Br J Clin Pharmacol.* 2021;87(2):237-255.
- Talebi Z, Sparreboom A, Colace SI. Pharmacogenomics in Cytotoxic Chemotherapy of Cancer. *Methods Mol Biol.* 2022;2547:63-94.
- Dong L, Jiang H, Kang Z, Guan M. Biomarkers for chemotherapy and drug resistance in the mismatch repair pathway. *Clin Chim Acta.* 2023;544:117338.
- Derouane F, van Marcke C, Berlière M, Gerday A, Fellah L, Leconte I, et al. Predictive Biomarkers of Response to Neoadjuvant Chemotherapy in Breast Cancer: Current and Future Perspectives for Precision Medicine. *Cancers (Basel).* 2022;14(16):3876.
- Generation Predictive Biomarkers for Immune Checkpoint Inhibitors in Cancer Patients. *Front Oncol.* 2021;11:683419.
- Ruiz-Bañobre J, Goel A. Genomic and epigenomic biomarkers in colorectal cancer: From diagnosis to therapy. *Adv Cancer Res.* 2021;151:231-304.
- Kwon MJ. Predictive biomarkers for molecularly targeted therapies and immunotherapies in breast cancer. *Arch Pharm Res.* 2022;45(9):597-617.
- Chung C. Predictive and prognostic biomarkers with therapeutic targets in colorectal cancer: A 2021 update on current development, evidence, and recommendation. *J Oncol Pharm Pract.* 2022;28(4):850-869.
- Kar A, Agarwal S, Singh A, Bajaj A, Dasgupta U. Insights into molecular mechanisms of chemotherapy resistance in cancer. *Transl Oncol.* 2024;42:101901.
- Al Saihati HA, Rabaan AA. Cellular resistance mechanisms in cancer and the new approaches to overcome resistance mechanisms chemotherapy. *Saudi Med J.* 2023;44(4):329-344.
- Dong L, Jiang H, Kang Z, Guan M. Biomarkers for chemotherapy and drug resistance in the mismatch repair pathway. *Clin Chim Acta.* 2023;544:117338.
- Tufail M, Cui J, Wu C. Breast cancer: molecular mechanisms of underlying resistance and therapeutic approaches. *Am J Cancer Res.* 2022;12(7):2920-2949.

13. Derouane F, van Marcke C, Berlière M, Gerday A, Fellah L, Leconte I, et al. Predictive Biomarkers of Response to Neoadjuvant Chemotherapy in Breast Cancer: Current and Future Perspectives for Precision Medicine. *Cancers (Basel)*. 2022;14(16):3876.
14. Tarighati E, Keivan H, Mahani H. A review of prognostic and predictive biomarkers in breast cancer. *Clin Exp Med*. 2023;23(1):1–16.
15. van den Ende NS, Nguyen AH, Jager A, Kok M, Debets R, van Deurzen CHM. Triple-Negative Breast Cancer and Predictive Markers of Response to Neoadjuvant Chemotherapy: A Systematic Review. *Int J Mol Sci*. 2023;24(3):2969.
16. Wang Z, Katsaros D, Biglia N, Shen Y, Fu Y, Loo LWM, et al. Predictive biomarkers in breast cancer: Current status and future perspectives. *Front Oncol*. 2023;13:1182945.
17. Maqbool M, Khan A, Shahzad A, Sarfraz Z, Sarfraz A, Aftab H, et al. Predictive biomarkers for colorectal cancer: a state-of-the-art systematic review. *Biomarkers*. 2023;28(6):562–598.
18. Pourali G, Khalili-Tanha G, Nazari E, Maftooh M, Nassiri MR, Hassanian SM, et al. Circulating Tumor Cells and Cell-free Nucleic Acids as Biomarkers in Colorectal Cancer. *Curr Pharm Des*. 2023;29(10):748–765.
19. Bhattacharya S. An empirical review on the resistance mechanisms of epidermal growth factor receptor inhibitors and predictive molecular biomarkers in colorectal cancer. *Crit Rev Oncol Hematol*. 2023;183:103916.
20. Lu X, Li Y, Li Y, Zhang X, Shi J, Feng H, et al. Prognostic and predictive biomarkers for anti-EGFR monoclonal antibody therapy in RAS wild-type metastatic colorectal cancer: a systematic review and meta-analysis. *BMC Cancer*. 2023;23(1):1117.
21. Odintsov I, Sholl LM. Prognostic and predictive biomarkers in non-small cell lung carcinoma. *Pathology*. 2024;56(2):192–204.
22. Chung C, Umore G. Prognostic and predictive biomarkers with therapeutic targets in nonsmall-cell lung cancer: A 2023 update on current development, evidence, and recommendation. *J Oncol Pharm Pract*. 2025;31(3):438–461.
23. Qian X, Meng QH. Circulating lung cancer biomarkers: From translational research to clinical practice. *Tumour Biol*. 2024;46(S1):S27–S33.
24. Restrepo JC, Martínez Guevara D, Pareja López A, Montenegro Palacios JF, Liscano Y. Identification and Application of Emerging Biomarkers in Treatment of Non-Small-Cell Lung Cancer: Systematic Review. *Cancers (Basel)*. 2024;16(13):2338.
25. Kim J, Kim HS, Nam M, Chae YK. Tissue-agnostic biomarkers in solid tumors: current approvals and emerging candidates. *Cancer Metastasis Rev*. 2025;44(3):58. doi:10.1007/s10555-025-10274-2.
26. Tripathy S, Gaur A, Jagadeb M, et al. Recent advances in detection techniques regarding predictive, prognostic, and diagnostic biomarkers in solid cancers and its future challenges. *Adv Cancer Res*. 2026;170:175–220. doi:10.1016/bs.acr.2025.12.006.
27. Kaczmarek F, Marcinkowska-Gapińska A, Bartkowiak-Wieczorek J, et al. Blood-based biomarkers as predictive and prognostic factors in immunotherapy-treated patients with solid tumors. *Cancers (Basel)*. 2025;17(12):2001. doi:10.3390/cancers17122001.
28. Puntambekar M, Shery N, Parokkaran I, Al-Hamas M. Predictive biomarkers in cancer immunotherapy: a narrative review across selected solid tumors. *Cureus*. 2025;17(7):e88647.
29. Odintsov I, Sholl LM. Prognostic and predictive biomarkers in non-small cell lung carcinoma. *Pathology*. 2024;56(2):192–204. doi:10.1016/j.pathol.2023.11.006.
30. Zhou Y, Tao L, Qiu J, et al. Tumor biomarkers for diagnosis, prognosis and targeted therapy. *Signal Transduct Target Ther*. 2024;9:132. doi:10.1038/s41392-024-01823-2.
31. Sato Y. Clinical utility of liquid biopsy-based companion diagnostics in non-small-cell lung cancer treatment. *Explor Target Antitumor Ther*. 2022;3(5):630–642. doi:10.37349/etat.2022.00104.
32. Janse van Rensburg HJ, Siu LL. Circulating biomarkers for therapeutic monitoring of anti-cancer agents. *Oncologist*. 2022;27(5):352–362.
33. Batis N, Brooks JM, Payne K. Lack of predictive tools for conventional and targeted cancer therapy: barriers to biomarker development and clinical translation. *Adv Drug Deliv Rev*. 2021;176:113854. doi:10.1016/j.addr.2021.113854.
34. Mestre-Ferrándiz J, et al. Expert-based collaborative analysis of the situation and prospects of biomarker test implementation in oncology in Spain. *Clin Transl Oncol*. 2024;26:985–990. doi:10.1007/s12094-023-03338-8.
35. Desai A, Lovly CM. Challenges in the implementation of ultrasensitive liquid biopsy approaches in precision oncology. *J Immunother Cancer*. 2023;11(6):e006793. doi:10.1136/jitc-2023-006793.
36. Lustberg MB, Stover DG, Chalmers JJ. Implementing liquid biopsies in clinical trials: state of affairs, opportunities and challenges. *Cancer J*. 2018;24(2):61–64. doi:10.1097/PPO.0000000000000309.
37. Derouane F, et al. Predictive biomarkers of response to neoadjuvant chemotherapy in breast cancer. *Cancers (Basel)*. 2022;14(16):3876.

- 38.Tarighati E, Keivan H, Mahani H. Prognostic and predictive biomarkers in breast cancer. Clin Exp Med. 2023;23:1–16.
- 39.Wang Z, et al. Predictive biomarkers in breast cancer: current status and future perspectives. Front Oncol. 2023;13:1182945.
- 40.van den Ende NS, et al. Triple-negative breast cancer and predictive markers. Int J Mol Sci. 2023;24:2969
- 41.Predictive Biomarkers of Response to Neoadjuvant Chemotherapy in Breast Cancer: Current and Future Perspectives for Precision Medicine. Cancers (Basel). 2022;14(16):3876. PMID: 36010869
- 42.Personalizing Cancer Therapy: The Role of Pharmacogenetics in Overcoming Drug Resistance and Toxicity. Expert Review of Precision Medicine and Drug Development. PMID: 40751817.