Review Article | Emerging Therapeutics

Advances in personalized medicine: translating genomic insights into targeted therapies for cancer treatment

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Background: Personalized medicine has revolutionized cancer treatment by utilizing genomic insights to tailor therapies based on individual molecular profiles. This approach enhances therapeutic efficacy, minimizes adverse effects, and addresses tumor heterogeneity through precision-targeted interventions.

Methods: A scoping review was conducted through a comprehensive literature search in PubMed, using MeSH terms and keywords related to genomic profiling and targeted cancer therapies. Eligible studies included original research involving cancer patients who underwent genomic profiling and targeted therapies from January 1, 1950, to February 9, 2025.

Results: Advances in next-generation sequencing (NGS) and bioinformatics have accelerated the identification of clinically relevant mutations—such as epidermal growth factor receptor (EGFR) in non-small cell lung cancer (NSCLC) and BRAF V600E in melanoma—enabling the development of effective targeted therapies. Emerging technologies like clustered regularly interspaced short palindromic repeats (CRISPR) gene editing and artificial intelligence (AI) are further refining treatment selection by enabling more precise and adaptive therapeutic strategies. Despite these innovations, challenges persist regarding data interpretation, equitable access, costs, regulatory frameworks, and integration into routine clinical workflows.

Conclusions: Genomic profiling is central to the advancement of precision oncology. The convergence of genomics, gene editing, and AI is paving the way toward more personalized, efficient, and inclusive cancer care. Realizing the full potential of personalized medicine will require interdisciplinary collaboration, investment in infrastructure, and ethical oversight to ensure broad, equitable, and responsible implementation in clinical practice.

Keywords: Personalized medicine; genomic profiling; targeted therapies; cancer treatment; next-generation sequencing (NGS)

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Introduction

Background

Personalized medicine has emerged as a revolutionary approach in modern healthcare, particularly in cancer treatment (1). Unlike traditional methods that rely on generalized treatment plans, personalized medicine leverages genomic insights to tailor therapies to an individual's genetic profile (1). This paradigm shift has been made possible by advances in genomic technologies, enabling more precise diagnoses and targeted therapeutic strategies that improve patient outcomes while minimizing adverse effects (2).

Cancer is a highly heterogeneous disease characterized by complex genetic and molecular variations among patients (3). The advent of next-generation sequencing (NGS) and other genomic profiling techniques has provided invaluable insights into the genetic mutations and alterations that drive tumor growth and progression (4). These advancements have paved the way for targeted therapies, which selectively inhibit specific molecular pathways involved in cancer development. By identifying actionable mutations, clinicians can prescribe treatments that are more effective for individual patients, thereby enhancing therapeutic efficacy and reducing unnecessary side effects (2).

Highlight box

Key findings

- Advances in genomic profiling and next-generation sequencing (NGS) have led to significant improvements in targeted cancer therapies, enhancing patient outcomes.
- Emerging technologies like clustered regularly interspaced short palindromic repeats (CRISPR) and artificial intelligence (AI) are refining personalized medicine by facilitating the identification of actionable mutations and optimizing treatment strategies.

What is known and what is new?

- Personalized medicine uses genomic insights to tailor therapies to individual genetic profiles, addressing cancer heterogeneity. Targeted therapies for known genetic drivers have improved survival rates. Integrating AI and machine learning into bioinformatics enhances data analysis and treatment selection, while CRISPR-based gene editing offers potential to correct specific mutations and develop innovative treatments.
- We propose a practical model integrating advanced genomics, CRISPR, and AI for personalized oncology. Emphasizing a multidisciplinary approach, we focus on transitioning new discoveries into routine care, overcoming data interpretation, access, and ethical barriers, and presenting actionable recommendations for broader adoption of personalized therapies.

What is the implication, and what should change now?

- The continued evolution of personalized medicine has the potential to transform cancer treatment paradigms, leading to more effective and individualized therapeutic options.
- Improved understanding of tumor genomics can guide clinical decision-making, ultimately enhancing patient care.
- Efforts should be made to increase accessibility to genomic testing and targeted therapies across diverse populations.
- Enhanced training for healthcare professionals in interpreting genomic data is essential to maximize the benefits of personalized medicine in clinical practice.

Rationale and knowledge gap

The integration of genomic technologies into oncology has led to significant improvements in patient care (5). Targeted therapies, such as tyrosine kinase inhibitors (TKIs) and monoclonal antibodies, have demonstrated superior efficacy in treating cancers with known genetic drivers (6,7). For example, epidermal growth factor receptor (EGFR) mutations in non-small cell lung cancer (NSCLC) can be effectively targeted using EGFR inhibitors (8), while HER2-positive breast cancers respond well to HER2-targeted therapies (9). Similarly, the identification of BRAF mutations in melanoma and KRAS mutations in colorectal cancer has enabled the development of highly specific therapeutic agents that significantly improve patient survival rates (10,11).

Beyond targeted therapies, emerging technologies such as clustered regularly interspaced short palindromic repeats (CRISPR) gene editing and AI are further refining the landscape of personalized medicine (12,13). CRISPR technology offers the potential to correct genetic mutations at the DNA level, opening new avenues for precision cancer treatment (12). AI and machine learning (ML) algorithms, on the other hand, are enhancing the interpretation of complex genomic data, facilitating the identification of novel biomarkers and optimizing treatment selection (13). These technological innovations are driving the transition from a one-size-fits-all approach to a more individualized treatment paradigm.

Objective

In this review, we discuss the role of genomic profiling in cancer treatment, highlighting its impact on therapy selection and patient outcomes. We also examine the challenges associated with accessibility, costs, and the need

Table 1 Search strategy

Items	Specification
Date of search	9 February, 2025
Database searched	PubMed
Search term used	("Genomics"[Mesh] OR "Genomic Profiling"[tiab] OR "Genomic Sequencing"[tiab] OR "NGS"[tiab] OR "Whole Exome Sequencing"[tiab] OR "Whole Genome Sequencing"[tiab] OR "Next-Generation Sequencing"[tiab]) AND ("Targeted Therap*"[tiab] OR "Targeted Treatment*"[tiab]) AND ("medical Oncology"[Mesh] OR "Cancer Therap*"[tiab] OR "Tumor Therap*"[tiab] OR "Cancer Treatment"[tiab] OR "Cancer Therap*"[tiab])
Timeframe	1950/01/01–2025/02/09
Inclusion and exclusion criteria	Inclusion criteria: (I) original research articles involving cancer patients undergoing genomic profiling and targeted therapies; (II) studies must examine genomic technologies, targeted therapies, tumor heterogeneity, resistance mechanisms, or emerging technologies such as CRISPR and AI; (III) studies must report patient outcomes, including survival or mortality
	Exclusion criteria: (I) non-original research articles, including reviews, commentaries, editorials, case reports, or opinion pieces; (II) studies conducted on non-cancer patient populations; (III) preclinical research lacking direct clinical relevance or studies that did not report patient outcomes; (IV) studies that did not assess genomic technologies in conjunction with targeted therapy
Selection process	Both authors were involved in reviewing and selecting the relevant literature

AI, artificial intelligence; CRISPR, clustered regularly interspaced short palindromic repeats.

for robust bioinformatics infrastructure. Additionally, we explore emerging solutions such as AI and gene-editing technologies and their role in shaping the evolving landscape of precision medicine. Finally, we outline the future directions of genomic-guided cancer therapy, emphasizing the ongoing advancements and collaborative efforts required to fully realize the potential of personalized medicine in oncology. We present this article in accordance with the PRISMA-ScR reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-25-34/rc).

Methods

We conducted a literature search in PubMed on February 9, 2025, using a combination of MeSH terms and free-text keywords to identify original studies investigating genomic profiling with clinical relevance in cancer patients. The full search strategy is detailed in *Table 1*, and *Figure 1* illustrates the study screening and selection process. The search covered the period from January 1, 1950 to February 9, 2025, with no language restrictions. Our PubMed search identified 238 studies. After screening titles and abstracts, 155 studies were excluded, leaving 83 studies for full-text review. Among these, 65 studies did not meet the inclusion criteria, and ultimately, 18 studies with clinical relevance were included in the review. The main findings of the 18 eligible studies are summarized in *Table 2*. Additionally, the risk of bias for the included studies was assessed using the Newcastle-Ottawa Scale (NOS).

Studies were included if they met the following criteria: (I) original research articles involving cancer patients undergoing genomic profiling and targeted therapies; (II) studies must examine genomic technologies, targeted therapies, tumor heterogeneity, resistance mechanisms, or emerging technologies such as CRISPR and AI; (III) studies must report patient outcomes, including survival or mortality.

Studies were excluded if they met any of the following criteria: (I) non-original research articles, including reviews, commentaries, editorials, case reports, or opinion pieces; (II) studies conducted on non-cancer patient populations; (III) preclinical research lacking direct clinical relevance or studies that did not report patient outcomes; (IV) studies that did not assess genomic technologies in conjunction with targeted therapy. Both authors reviewed the retrieved studies to assess their relevance. Discrepancies were resolved through discussion.

Results

Genomic technologies and the role of bioinformatics in data analysis

Epigenomics and phenomics data along with genomic

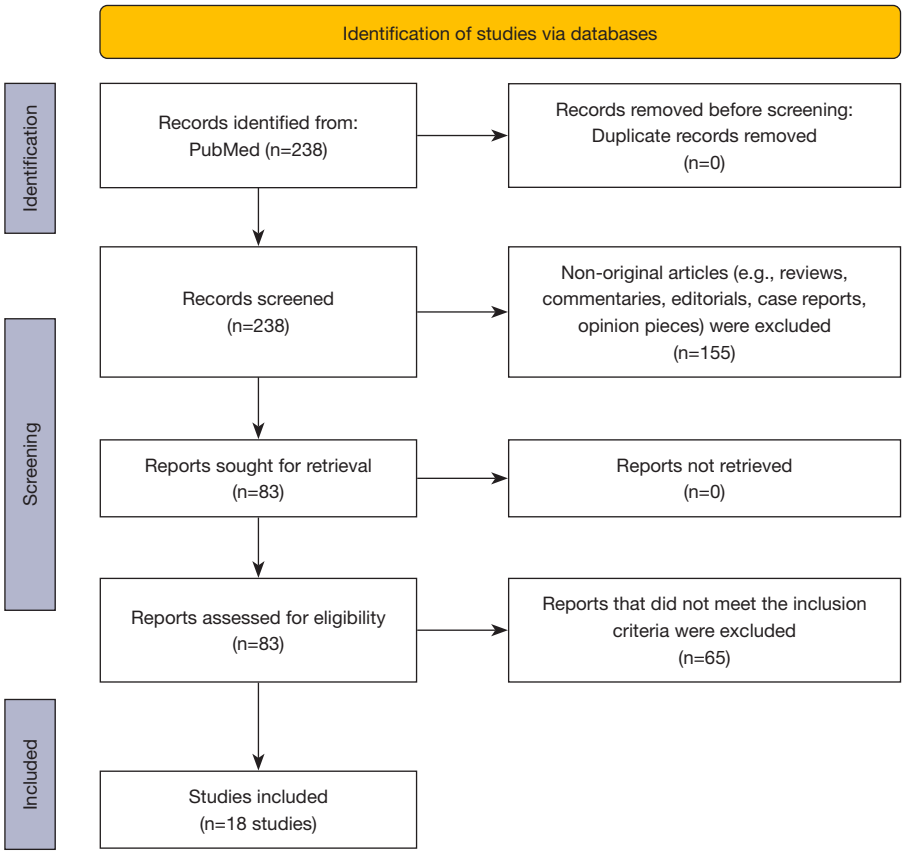

Figure 1 PRISMA flow diagram depicting study screening and selection process.

technologies have become cornerstone tools in advancing personalized medicine. They have revolutionized our understanding and treatment of diseases, especially cancer (1,32). By enabling detailed analysis of an individual's genetic makeup, these technologies provide critical insights into the molecular underpinnings of health and disease. Through high-throughput sequencing methods such as NGS, including targeted sequencing panels (TSP), whole exome sequencing (WES), and whole genome sequencing (WGS), researchers can identify specific genetic mutations and alterations that drive tumor development and progression (*Figure 2*) (4).

This wealth of genomic data empowers clinicians to tailor treatment strategies to each patient's unique genetic profile, enhancing therapeutic efficacy while minimizing adverse effects. As a result, genomic technologies not only facilitate more precise diagnoses but also pave the way for innovative targeted therapies that hold great promise in transforming patient care within the realm of personalized medicine. In the following, we will provide a brief overview of these different sequencing techniques, highlighting their principles, applications, and significance in advancing personalized medicine. Additionally, we will mention some significant examples that illustrate how these technologies have been successfully applied in clinical settings to improve patient outcomes.

NGS has revolutionized genomic research by enabling rapid and cost-effective sequencing of DNA. Unlike traditional Sanger sequencing, which processes one sequence at a time, NGS can analyze millions of DNA fragments simultaneously (33). This parallel processing capability significantly enhances throughput and reduces costs, making it an invaluable tool for cancer genomics. The applications of NGS in oncology are vast. It facilitates comprehensive tumor profiling, enabling researchers to identify mutations, copy number variations, and other genomic alterations that drive cancer progression and clinical judgment in patients (34). Different platforms exist within the NGS landscape, such as Illumina's sequencing technology and Ion Torrent's

Table 2 Impact of genomic profiling on cancer treatment decisions and clinical outcomes

Study	Design	Risk of bias	Cancer type	Genomic profiling method	Key findings	Clinical significance
Tsimberidou *et al.*, 2017 (14)	Retrospective	Moderate	Advanced cancer (n=1,436)	Comprehensive genomic profiling (CGP)	637 patients had actionable aberrations; those receiving molecularly targeted therapy (MTT, n=390) had improved response rates (11% *vs.* 5%; P=0.0099), longer failure-free survival (3.4 *vs.* 2.9 months; P=0.0015), and longer overall survival (8.4 *vs.* 7.3 months; P=0.041) compared to unmatched patients. However, targeting only the PI3K pathway did not improve outcomes	Highlights the clinical benefit of CGP-driven MTT but underscores the need for multi-pathway targeting in PI3K-altered tumors
Leroy *et al.*, 2023 (15)	Retrospective	Low	Various cancers (n=416)	NGS-based CGP	75% had actionable mutations; treatment modification occurred in 17.3%, more frequently in metastatic disease (OR =2.73, 95% CI: 1.31–5.71, P=0.007). Genomic-directed treatment changes were most common within 6 months but extended up to 24 months post-testing	Supports CGP utility in guiding treatment decisions, particularly in metastatic settings
Hughes *et al.*, 2022 (16)	Retrospective	Low	NSCLC (n=248)	NGS and biomarker testing	76% of metastatic NSCLC patients received first-line therapy. Median OS: 9.0 months (95% CI: 6.5–11.6). Targeted therapy significantly improved OS (28.7 *vs.* 6.6 months; P<0.001)	Highlights the need for comprehensive genomic profiling and early diagnosis in young NSCLC patients
Kim *et al.*, 2023 (17)	Prospective	Moderate	NSCLC (n=152)	ctDNA *vs.* tissue sequencing	High cfDNA concentration at diagnosis was associated with poorer overall survival. The sensitivity and precision of ctDNA analysis compared to tissue sequencing were 58.4% and 61.5%, respectively	ctDNA shows prognostic value in NSCLC, but its lower sensitivity and precision limit its standalone use
Okamura *et al.*, 2021 (18)	Retrospective	Low	Biliary tract cancer (n=121)	ctDNA-based profiling	Concordance between ctDNA and metastatic site tissue-DNA was higher than with primary tumor DNA. Molecularly matched therapy led to significantly longer progression-free survival (HR: 0.60, 95% CI: 0.37–0.99, P=0.047) and a higher disease control rate (61% *vs.* 35%, P=0.04) compared to unmatched regimens	ctDNA profiling aids treatment selection and improves outcomes in biliary tract cancer
Harttrampf *et al.*, 2017 (19)	Prospective	Moderate	Pediatric refractory tumors (n=75)	Comparative genomic hybridization array, NGS, whole-exome and RNA sequencing	Molecular analysis identified actionable alterations in 60.9% of patients, leading to treatment modifications in 14 cases. Diagnosis was revised in three patients	Comprehensive genomic profiling is feasible in pediatric refractory tumors and reveals clinically relevant alterations, but access to targeted therapies remains a challenge
Riedl *et al.*, 2021 (20)	Prospective	High	Advanced carcinoma (n=24)	ctDNA *vs.* tissue profiling	Matched treatments were identified in 46% of patients, but the median PFS ratio was <1.2 in all cases, leading to study termination. Combination therapy options were suggested in most cases	The study underscores the challenges of implementing ctDNA-driven precision oncology, highlighting the need for improved patient selection and optimized treatment matching strategies

Table 2 (*continued*)

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Study	Design	Risk of bias	Cancer type	Genomic profiling method	Key findings	Clinical significance
Pleasance *et al.*, 2022 (21)	Retrospective	Moderate	Advanced cancer (n=570)	WGTA	Clinically actionable targets were identified in 83% of patients, with 37% receiving WGTA-informed treatments. RNA expression data contributed to 67% of treatment decisions, with 25% based solely on RNA data. Clinical benefit was observed in 46% of WGTA-informed treatments	WGTA enhances treatment selection by integrating RNA expression and genomic data, expanding therapeutic options beyond standard sequencing
Ding *et al.*, 2021 (22)	Retrospective	High	Lung cancer (n=12)	WES and RNA sequencing	Neoantigen vaccine therapy showed a 25% objective response rate and 75% disease control rate, with a median PFS of 5.5 months and OS of 7.9 months. All adverse events were grade 1–2	Neoantigen-based vaccines demonstrate feasibility and safety in lung cancer, warranting further investigation for broader clinical application
Yuan *et al.*, 2017 (23)	Retrospective	High	Metastatic breast cancer (n=44)	NGS	Actionable mutations were identified in 95% of patients, and 55% of those with actionable mutations received targeted therapy, with 70% showing assessable responses	Early NGS in MBC can uncover actionable targets and guide treatment, supporting its integration into clinical decision-making
Prager *et al.*, 2019 (24)	Prospective	Moderate	Various cancers (n=55)	NGS	Molecular profiling-guided therapy led to longer PFS in 62% of patients, with a median PFS improvement from 61 to 112 days (P=0.002). Disease control was achieved in 56% of patients, and median OS was 348 days	Real-time molecular profiling enhances treatment personalization, leading to improved clinical outcomes and prolonged survival in selected patients
Dang *et al.*, 2024 (25)	Retrospective	Moderate	Various cancers (n=94)	NGS	Actionable mutations were identified in 53.6% of patients. Among those, 11 received molecularly guided therapy. The PFS2/PFS1 ratio was ≥1.3 in 62.5% of evaluable patients, and median OS was 7.3 months	Molecular profiling informs targeted therapy decisions, but limited uptake of recommended treatments highlights challenges in clinical implementation
Dalens *et al.*, 2023 (26)	Prospective	Moderate	Lung cancer (n=135)	WES	Certain germline SNPs in immunity-related genes negatively impacted survival on EGFR TKI treatment. SNPs in HLA-DRB5, KIR3DL1, and KIR3DL2 were linked to reduced PFS and OS	Highlights the role of germline variations in treatment response, suggesting potential biomarkers for refining targeted therapies
Martínez-Herrera *et al.*, 2024 (27)	Retrospective	Low	NSCLC (n=127)	NGS	32.3% of EGFR-negative patients had other actionable mutations (e.g., ALK, BRAF, ROS1, RET), supporting early targeted therapy. ALK and EGFR mutations were significantly associated with OS, while ALK, TMB, and brain MRI findings were linked to PFS	Emphasizes the necessity of comprehensive NGS in NSCLC, particularly in resource-limited settings, to optimize treatment strategies and improve patient outcomes

Table 2 (*continued*)

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Study	Design	Risk of bias	Cancer type	Genomic profiling method	Key findings	Clinical significance
Gouton *et al.*, 2022 (28)	Retrospective	Moderate	Solid tumors (n=191)	cfDNA genomic profiling	AMAs found in 52% of patients; most common alterations: TP53 (52%), KRAS (14%), DNMT3 (11%). Most common AMAs: CHEK2 (10%), PIK3CA (9%), ATM (7%). No significant difference in PFS (2.66 *vs.* 3.81 months, P=0.17), OS (5.3 *vs.* 7.1 months, P=0.64), or PFS2/PFS1 ratio ≥ 1.3 (20% *vs.* 24%, P=0.72) between MMT and non-MMT groups. MMT group: ORR 19%, disease control rate 32%	Feasibility of cfDNA profiling confirmed, but no clear survival benefit in unselected pan-cancer patients
Kim *et al.*, 2022 (29)	Prospective	Low	Metastatic colorectal cancer (n=272)	Longitudinal ctDNA monitoring	Detectable ctDNA mutations in 90.3% of patients before treatment. ctDNA clearance post-chemotherapy correlated with longer PFS (adjusted HR: 0.22, 95% CI: 0.10–0.46). ctDNA progression preceded radiological PD in 58.1% (median 3.3 months). Resistant mutations (34.9%) and gene amplification (7.0%) detected at PD. Newly identified mutations in 16.3% of PD patients were potential candidates for targeted therapy	Supports ctDNA monitoring as a tool for early progression detection and guiding personalized treatment in metastatic CRC
Lin *et al.*, 2020 (30)	Retrospective	Low	NSCLC (EGFR/ALK wild-type) (n=198)	TMB analysis by NGS	In EGFR-mutant patients treated with first-generation EGFR-TKIs, TMB-L group had significantly longer PFS (16.4 *vs.* 9.0 *vs.* 7.4 months; log-rank P=0.006). In EGFR/ALK wild-type patients receiving pemetrexed/platinum, the TMB-L group had a superior ORR (53.8% *vs.* 23% *vs.* 8.3%; log-rank P=0.037) and numerically longer PFS (6.9 *vs.* 4.3 *vs.* 4.6 months; P=0.22)	Highlights TMB as a potential biomarker influencing response to EGFR-TKIs and chemotherapy in NSCLC, though larger studies are needed for validation
Canino *et al.*, 2024 (31)	Retrospective	Moderate	Metastatic breast cancer (n=101)	NGS	75% had at least one actionable mutation. Nine received targeted therapy: eight with PIK3CA mutations received alpelisib/fulvestrant, and one with FGFR1/2 amplifications received TAS120. Median PFS for treated patients was 3.8 months. NGS results influenced therapy in 9% of cases	Highlights the potential of NGS in guiding treatment decisions for metastatic breast cancer, though limited sample size and follow-up suggest the need for further validation

ALK, anaplastic lymphoma kinase; AMA, actionable molecular alteration; CI, confidence interval; CGP, comprehensive genomic profiling; cfDNA, cell-free DNA; CRC, colorectal cancer; ctDNA, circulating tumor DNA; EGFR, epidermal growth factor receptor; EGFR-TKI, epidermal growth factor receptor tyrosine kinase inhibitor; FGFR, fibroblast growth factor receptor; HR, hazard ratio; MTT, molecularly targeted therapy; NGS, next-generation sequencing; NSCLC, non-small cell lung cancer; OR, odds ratio; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PI3K, phosphatidylinositol 3-kinase; RET, rearranged during transfection; ROS1, ROS proto-oncogene 1; SNP, single nucleotide polymorphism; TKI, tyrosine kinase inhibitor; TMB, tumor mutational burden; WES, whole-exome sequencing; WGTA, whole-genome and transcriptome analysis.

semiconductor-based approach (35). These platforms have been instrumental in deciphering complex cancer genomes and guiding personalized treatment strategies. In particular, standardization in NGS workflow including template preparation (library preparation and amplification), sequencing, imaging, and data analysis has helped to increase the accuracy in data assembly and quality. However, the development of robust state-of-the-art bioinformatics pipelines to extract meaningful biological insights is still a significant topic (35).

TS panels are specialized tools used in genomics to analyze specific regions of DNA, allowing researchers to focus on a selected number of genes or genomic areas of interest for diagnosis, prognosis, and treatment monitoring (36). These panels contain a curated set of probes designed to capture and enrich targeted sequences (regions of interest),

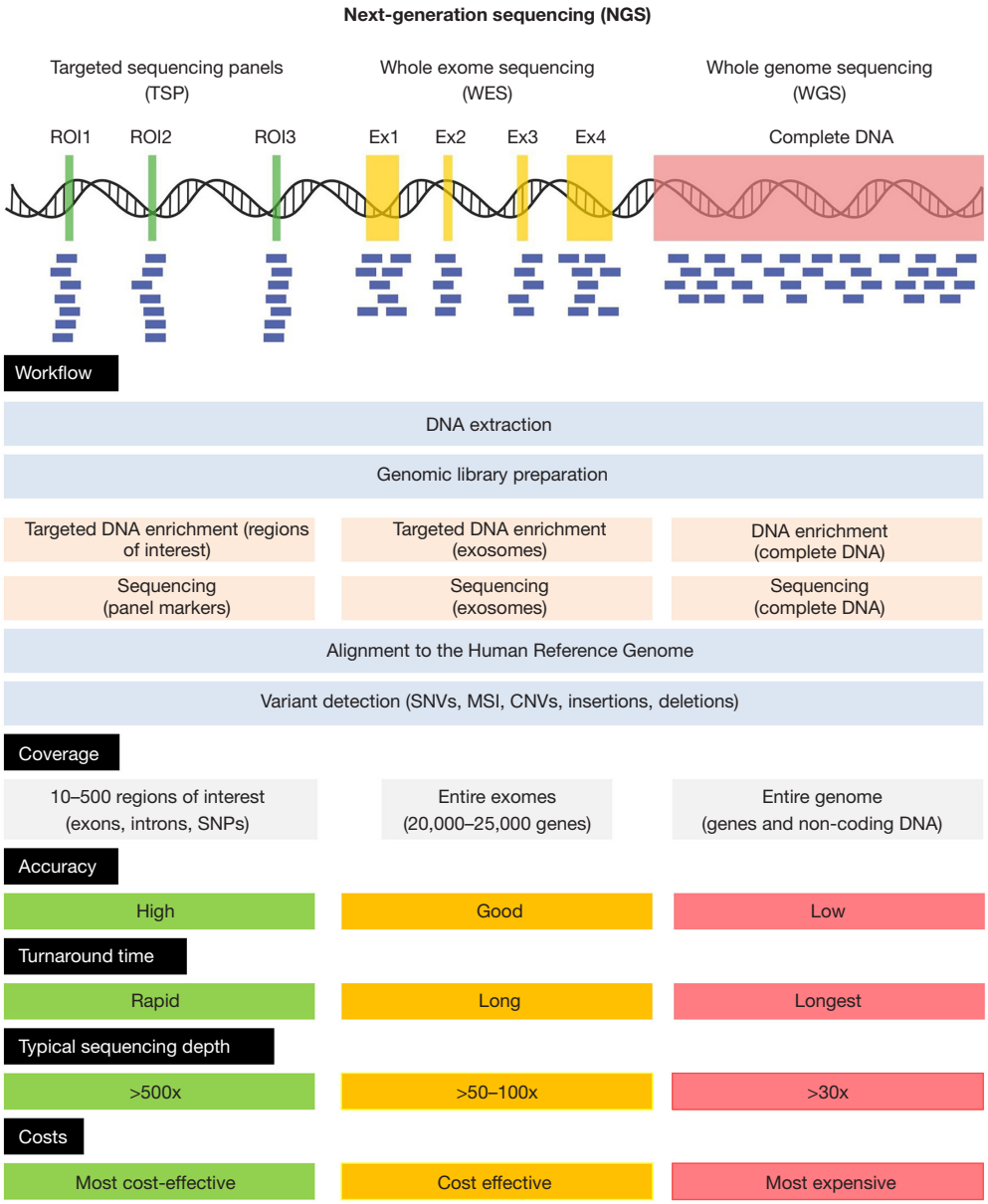

Figure 2 Overview of the key sequencing technologies utilized in personalized medicine. TSP, WES, and WGS are next-generation sequencing techniques with specific workflows. They involve DNA extraction, library preparation, DNA enrichment (regions of interest, exomes, or complete DNA), sequencing, and data analysis to identify regions with SNVs, MSI, CNVs, insertions, or deletions. These methods differ in coverage, accuracy, turnaround time, sequencing depth, and costs. CNVs, copy number variants; Ex, exon; MSI, microsatellite instability; ROI, region of interest; SNVs, single nucleotide variants; TSP, targeted sequencing panels; WES, whole exome sequencing; WGS, whole genome sequencing.

making it easier to identify variations such as single nucleotide polymorphisms (SNPs), insertions, deletions, and other genetic alterations associated with diseases. By concentrating on particular targets, these panels enhance the efficiency and accuracy of sequencing workflows while reducing costs and data complexity compared to whole-genome sequencing (37-39). They are widely used in clinical diagnostics, cancer research, and personalized

medicine.

WES focuses specifically on the exons, which make up approximately 1.5% of the human genome but contain around 85% of known monogenic, disease-related variants (40). WES is particularly advantageous for identifying unbiased clinically relevant mutations and copy number alterations associated with various cancers (41). One notable example is its application in hereditary breast and ovarian cancer syndrome research, where WES has successfully identified pathogenic variants in genes such as BRCA1 and BRCA2. By concentrating on exonic regions, WES provides a cost-effective means to uncover significant genetic alterations that can inform therapeutic decisions (42).

WGS offers a more comprehensive analysis by sequencing the entire genome, including both coding and non-coding regions. The unique capabilities of WGS allow for the detection of structural variants, copy number variations, and regulatory elements that may play critical roles in tumor behavior. While WGS generates a vast amount of data compared to WES or TSP, its sensitivity enables researchers to uncover hidden complexities within cancer genomes. For instance, studies have demonstrated how WGS combined with specialized bioinformatics pipelines can detect novel fusion genes or previously unrecognized mutations that contribute to drug resistance or tumor recurrence (43,44). The breadth of information obtained from WGS positions it as a powerful tool in understanding cancer biology at an unprecedented level. Furthermore, combining the comprehensive genomic data of specific tumor types with detailed clinical information will create a groundbreaking research platform. This will enable a deeper understanding of the mechanisms behind treatment response, resistance development, and treatment failure. Ultimately, this approach will help identify unique characteristics of individual cancer genomes and facilitate the development of targeted cancer therapies (45,46).

It is evident that bioinformatics plays a pivotal role in the realm of personalized medicine, serving as the bridge between complex genomic data and actionable clinical insights. As advancements in sequencing technologies continue to evolve and produce vast amounts of 'big data', bioinformatics provides the necessary tools and methodologies to analyze, interpret, and integrate this information effectively (47). The primary objective is to translate raw genetic information into meaningful knowledge that can guide clinical personalized decision-making and improve patient outcomes (48). An exemplar Bioinformatics Multidrug Combination Protocol for Personalized Precision Medicine was developed for breast cancer patients. This protocol enables personalized drug combinations extracted from hundreds of drugs and thousands of drug combinations, offering more effective treatment options (49). The protocol integrates an individual pattern of perturbed gene expression for each patient, similar to a fingerprint, containing gene expression profiles different from healthy individuals. The algorithm can then extract an accurate personalized drug treatment, producing a more beneficial therapeutic effect in the respective patient (49).

At the heart of bioinformatics lies the data analysis pipeline, which includes several critical steps from sequencing to interpretation (*Figure 3*). Initially, raw sequencing data undergo quality control measures to filter out low-quality reads that could introduce errors into subsequent analyses (46,50). Following this step, the cleaned data is aligned against reference genomes using sophisticated pipelines such as the Burrows-Wheeler Aligner (BWA), Bowtie2, HISAT, or LongStrain (51-53). This alignment process is crucial for identifying genetic variants like SNPs, insertions, or deletions that may play a significant role in disease development. Variant calling is then performed using software like the Genome Analytic Tool Kit (GATK) or SAMtools to accurately identify these genetic alterations (54,55).

Once variants are identified, bioinformatics tools facilitate their annotation and interpretation through cross-referencing with established databases like the Catalogue of Somatic Mutations in Cancer (56) for cancer-related mutations or dbSNP for known polymorphisms. These resources provide context regarding whether specific mutations have been previously associated with clinical outcomes or biological functions related to cancer pathogenesis. Functional impact prediction tools such as Sorting Intolerant From Tolerant (57) or Polymorphism Phenotyping (58) further aid in assessing whether specific mutations are likely to affect protein function, thereby guiding therapeutic decisions.

Moreover, bioinformatics enables integrative genomics, by combing genomic data with other omics layers, such as transcriptomics and proteomics, to provide a comprehensive view of tumor biology. This approach allows researchers to uncover intricate interactions between genetic alterations and gene expression profiles influenced by environmental factors or treatment modalities. For example, understanding how specific mutations correlate with differential gene expression patterns can lead to more targeted therapeutic

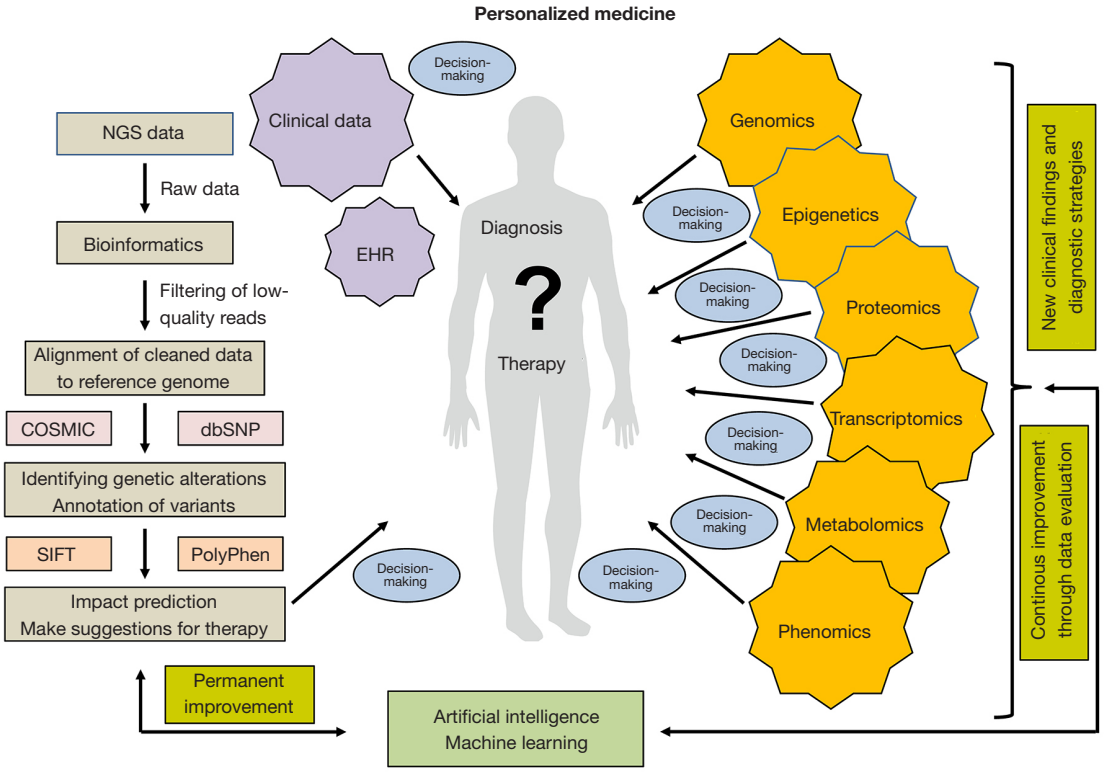

Figure 3 Integration of bioinformatics pipelines in personalized medicine. This diagram shows the bioinformatics pipelines that convert raw sequencing data into actionable clinical insights for decision-making in personalized medicine. Key steps include quality control to remove low-quality reads, aligning cleaned data to reference genomes, variant calling to identify genetic alterations, and annotation to provide context to variants using databases like COSMIC, dbSNP, and tools like SIFT, PolyPhen, and others for predicting functional impact. Additionally, the figure demonstrates how integrative genomics combines genomics, transcriptomics, and proteomics to offer a holistic view of tumor biology. Bioinformatics is crucial in interpreting complex genomic data and guiding personalized therapeutic decisions in cancer treatment by combining this data with patient-specific clinical and electronic health records. EHR, electronic health record(s); NGS, next-generation sequencing; SIFT, Sorting Intolerant From Tolerant.

strategies customized for individual patients (45,46).

ML and AI are making significant progress in bioinformatics, providing innovative solutions for analyzing high-dimensional datasets produced by modern sequencing technologies and influencing clinical decision-making (13,59). These advanced computational techniques can detect patterns within genomic data that traditional analytical methods may overlook. By utilizing ML algorithms, researchers can forecast patient responses using their individual genomic profiles and uncover new biomarkers linked to treatment effectiveness or resistance. However, despite its tremendous potential benefits, bioinformatics faces several challenges that must be addressed to fully realize its promise in personalized medicine. Issues surrounding data storage capacity requirements arise due to the massive volumes of genomic data generated daily, thus necessitating robust infrastructure capable of supporting efficient access and processing capabilities. Additionally, ensuring reproducibility and accuracy throughout analyses conducted across varying contexts remains paramount for establishing trust in bioinformatic findings. Moreover, although AI has rapidly revolutionized diagnosis, prognosis, treatment, and prevention in oncology and related fields, there are also concerns about biases inherent in algorithms, reflecting the unconscious biases of their creators (60). Nevertheless, bioinformatics serves as an essential pillar supporting personalized medicine by transforming complex genomic

data into actionable insights that inform clinical practice and pave new pathways toward improved patient care experiences overall.

Looking ahead, future directions in bioinformatics will focus on developing user-friendly interfaces and automating routine tasks to minimize barriers for clinicians seeking expertise in genomic analysis. Efforts aimed at enhancing collaboration between computational scientists and healthcare professionals will foster an environment conducive to translating genomic insights into real-world applications ultimately benefiting patients navigating complex diseases like cancer.

Key genomic alterations and targeted therapies in cancer

Advances in NGS and biomarker-driven approaches have led to improved clinical outcomes in multiple malignancies. *Table 3* summarizes key genomic alterations identified through genomic profiling, their associated cancer types, Food and Drug Administration (FDA)-approved or investigational targeted therapies, and their clinical significance.

Certain genomic alterations serve as crucial therapeutic targets across multiple malignancies. In NSCLC, EGFR mutations (L858R, exon 19 deletions, T790M) drive tumor growth through aberrant activation of the EGFR signaling pathway, making them prime candidates for EGFR TKIs (17,30). Similarly, ALK rearrangements and ROS1 fusions in NSCLC (62) define subsets of patients who benefit from ALK and ROS1 inhibitors, respectively (16,63).

In colorectal, melanoma, and thyroid cancers, BRAF V600E mutations lead to constitutive activation of the MAPK pathway, rendering tumors susceptible to BRAF/MEK inhibition (66,86). KRAS G12C mutations, once deemed undruggable, have become actionable with recent advancements in KRAS inhibitors, although other KRAS variants remain under investigation (64,65).

In breast and gastric cancers, HER2 (ERBB2) amplification is a well-characterized oncogenic driver, guiding the use of HER2-targeted therapies (71,72). PIK3CA mutations, particularly in hormone receptor-positive (HR+)/HER2-negative breast cancer, are associated with PI3K/AKT pathway activation and response to PI3K inhibitors (31,64,69,87,88).

Another emerging class of actionable alterations includes tumors with high microsatellite instability (MSI-H) and deficient mismatch repair (dMMR) (67,72). These tumors, found in colorectal, endometrial, and other malignancies, exhibit high mutation burdens and respond exceptionally well to immune checkpoint inhibitors, leading to tumor-agnostic FDA approvals (72,80). In hematologic cancers, mutations in JAK2 (p.V617F) and JAK3 drive myeloproliferative neoplasms, with JAK inhibitors demonstrating significant clinical benefit (89,90). Similarly, MET amplification and exon 14 skipping mutations in NSCLC have emerged as critical therapeutic targets (91). Rare but clinically significant alterations, such as NTRK gene fusions, occur across various solid tumors and have led to the development of tissue-agnostic therapies with durable response rates (84).

While genomic profiling has significantly improved treatment stratification, not all mutations translate into therapeutic success. TP53 mutations, prevalent in multiple cancers, remain challenging due to the lack of direct targeting strategies. However, they provide valuable prognostic information and guide treatment selection (72,75-79).

Clinical significance of genomic profiling in oncology

Genomic profiling has revolutionized patient outcomes by enabling personalized therapy selection and identifying prognostic biomarkers. *Tables 2,3* summarize the clinical significance of various genomic profiling methods, including NGS, comprehensive genomic profiling (CGP), WES, and circulating tumor DNA (ctDNA) analysis.

Multiple studies confirm that genomic profiling facilitates the identification of actionable mutations, leading to improved treatment responses. For instance, Tsimberidou *et al.* (14) demonstrated that molecularly targeted therapy (MTT) based on CGP led to significantly longer failure-free survival (3.4 *vs.* 2.9 months; P=0.002) and overall survival (OS) (8.4 *vs.* 7.3 months; P=0.04). Similarly, Prager *et al.* (24) showed that NGS-based molecular profiling extended progression-free survival (PFS) from 61 to 112 days (P=0.002), reinforcing the role of personalized treatment selection.

In NSCLC, Hughes *et al.* (16) reported that patients who received targeted therapy had a dramatically improved median OS of 28.7 months compared to 6.6 months for those without targeted options (P<0.001). These findings highlight the necessity of early genomic testing to ensure that eligible patients benefit from precision medicine.

On these grounds, ctDNA analysis offers a minimally invasive alternative for tumor profiling, particularly for patients with insufficient tissue samples. Kim *et al.* (17)

Table 3 Key genomic alterations and their clinical implications in cancer

Gene/mutation	Cancer type	Targeted therapy	Clinical significance
EGFR mutations (L858R, Exon 19 deletions, T790M) (17,30,61)	NSCLC	Osimertinib, erlotinib, gefitinib	FDA-approved targeted therapies. Osimertinib is the standard of care for T790M-positive cases
ALK rearrangements (16,62,63)	NSCLC	Crizotinib, alectinib, lorlatinib	ALK inhibitors significantly prolong survival in ALK-positive NSCLC, with alectinib showing superior efficacy over crizotinib as a first-line therapy
KRAS mutations (G12C, G12D, G13D) (64,65)	NSCLC (G12C), colorectal cancer (investigational), pancreatic cancer (investigational)	Approved: sotorasib, adagrasib (for KRAS G12C-mutant NSCLC). Investigational: MEK inhibitors, pan-KRAS inhibitors for other KRAS mutations	KRAS G12C inhibitors are the first FDA-approved therapies for NSCLC. Other KRAS mutations remain under study
BRAF V600E (66-68)	Melanoma, colorectal cancer, thyroid cancer	Dabrafenib + trametinib, encorafenib + cetuximab	FDA-approved combination therapies, with dual BRAF/MEK inhibition being the preferred approach
PIK3CA mutations (31,48,64,69,70)	Breast cancer, colorectal cancer	Approved: alpelisib + fulvestrant (for HR+/HER2− breast cancer). Investigational: mTOR inhibitors in PIK3CA-mutant tumors	Alpelisib is FDA-approved for HR+/HER2− breast cancer. mTOR inhibitors are used in broader settings but not directly for PIK3CA mutations
HER2 (ERBB2) amplification/ mutation (71-74)	Breast cancer, gastric cancer, NSCLC (HER2-mutant)	Trastuzumab, lapatinib, trastuzumab-deruxtecan (T-DXd, for NSCLC HER2 mutations)	Standard therapy for HER2+ tumors. T-DXd is FDA-approved for HER2-mutant NSCLC
TP53 mutations (72,75-79)	Various cancers	No direct targeted therapy	Associated with poor prognosis, resistance to therapy
MSI-H/dMMR (67,72,80)	Colorectal, endometrial, gastric cancer	Pembrolizumab, nivolumab	First FDA-approved biomarker-based therapy. Approved for MSI-H tumors regardless of origin
JAK2 p.V617F, JAK3 mutations (81,82)	Myeloproliferative neoplasms, hematologic malignancies	JAK inhibitors (ruxolitinib, fedratinib for myeloproliferative neoplasms); potential role in immunotherapy response for NSCLC (research phase)	JAK2 inhibitors are FDA-approved for MPNs. JAK3 mutations are under investigation for immunotherapy sensitivity
MET amplification, HER2 overexpression (73,83)	Lung cancer	Capmatinib, tepotinib, crizotinib (for MET amplification); HER2-targeted therapies for HER2 overexpression	MET exon 14 skipping and HER2-mutant NSCLC are FDA-approved targets for therapy. MET amplification is still under investigation
NTRK fusions (84,85)	Solid tumors	Larotrectinib, entrectinib	High response rates to TRK inhibitors. Approved for any $NTRK^+$ tumor

ALK, anaplastic lymphoma kinase; BRAF, v-Raf murine sarcoma viral oncogene homolog B; dMMR, deficient mismatch repair; EGFR, epidermal growth factor receptor; FDA, Food and Drug Administration; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; JAK, Janus kinase; KRAS, Kirsten rat sarcoma viral oncogene homolog; MEK, mitogen-activated protein kinase kinase; MET, mesenchymalepithelial transition; MPN, myeloproliferative neoplasm; MSI-H, microsatellite instability-high; mTOR, mechanistic target of rapamycin; NSCLC, nonsmall cell lung cancer; NTRK, neurotrophic receptor tyrosine kinase; PIK3CA, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; T-DXd, trastuzumab-deruxtecan; TP53, tumor protein p53; TRK, tropomycin receptor kinase.

demonstrated that ctDNA had prognostic value in NSCLC, with high cell-free DNA (cfDNA) concentrations at diagnosis correlating with poorer survival. Similarly, Okamura *et al.* (18) showed that ctDNA profiling in biliary tract cancer led to significantly longer PFS (HR: 0.60, P=0.047) and a higher disease control rate (61% *vs.* 35%, P=0.04) when using molecularly matched therapy. However, despite its promise, liquid biopsy faces challenges. Riedl *et al.* (20) reported that matched treatment based on ctDNA findings did not result in meaningful PFS improvement, with a median PFS ratio of <1.2 in all cases. Similarly, Gouton *et al.* (28) found no significant survival difference between patients who received molecularly matched therapy and those who did not (PFS: 2.66 *vs.* 3.81 months, P=0.17). These findings suggest that while ctDNA profiling is valuable, its predictive accuracy and clinical application need refinement.

Beyond DNA mutation analysis, incorporating RNA expression data has been shown to enhance treatment stratification. Pleasance *et al.* (21) found that whole-genome and transcriptome analysis (WGTA) identified clinically actionable targets in 83% of advanced cancer patients, with 37% receiving WGTA-informed treatments. RNA expression data contributed to 67% of treatment decisions, highlighting its added value over DNA-based methods alone.

Neoantigen-based therapies also benefit from genomic profiling. Ding *et al.* (22) investigated whole-exome sequencing and RNA sequencing to guide neoantigen vaccine development in lung cancer, reporting a 25% objective response rate, 75% disease control rate, and a median OS of 7.9 months. These findings suggest that integrating genomic profiling into immunotherapy selection could further personalize treatment approaches. TMB has emerged as a potential biomarker for therapy response. Lin *et al.* (30) demonstrated that in EGFR-mutant NSCLC, patients with low TMB had significantly better PFS (16.4 *vs.* 9.0 *vs.* 7.4 months, P=0.006) on first-generation EGFR-TKIs. Similarly, in EGFR/ALK wild-type NSCLC patients treated with chemotherapy, those with low TMB had a superior objective response rate (53.8% *vs.* 23% *vs.* 8.3%, P=0.037), though PFS improvement was not statistically significant. These findings suggest that TMB could serve as a biomarker to refine treatment selection in lung cancer.

Challenges in real-world implementation

Despite the transformative role of genomic profiling in oncology, several real-world challenges hinder its widespread implementation. In particular, access to genomic testing remains highly variable across regions and healthcare systems (19,76,92). In low- and middle-income countries (LMICs), limited infrastructure, high costs, and absent reimbursement policies significantly restrict the availability of molecular diagnostics. Even in high-income countries, disparities exist between well-equipped academic centers and community hospitals with fewer resources. Martínez-Herrera *et al.* (27) emphasized this inequity by showing that 32.3% of EGFR-negative NSCLC patients in underserved areas harbored other actionable mutations that would have gone undetected without access to comprehensive NGS.

Germline profiling, though potentially valuable in predicting treatment response, remains underutilized. Dalens *et al.* (26) reported that certain germline SNPs in immunity-related genes negatively impacted survival in patients receiving EGFR TKI therapy. However, ethical concerns, unclear regulatory frameworks, and minimal integration into routine clinical workflows have limited its application. Standardized guidelines and further research are necessary to incorporate germline data effectively into precision oncology.

Interpreting complex genomic data is another major barrier for both oncologists and patients. Thavaneswaran *et al.* (93) found that while most oncologists referred patients for CGP, their confidence in interpreting and communicating these results was moderate, and significantly lower for germline findings. Similarly, Bylstra *et al.* (94) noted that patients often struggled to understand genomic information, while clinicians cited time constraints as a barrier to effective communication. These findings underscore the need for enhanced clinical training, robust decision-support tools, and accessible patient education materials to bridge the genomic literacy gap.

Furthermore, not all genomic findings translate into improved clinical outcomes. Dang *et al.* (25) observed that although 53.6% of patients had actionable alterations, only 11 received molecularly guided therapy, highlighting a significant gap between molecular insights and treatment implementation. Similarly, in pediatric oncology, Harttrampf *et al.* (19) found that while 60.9% of refractory pediatric tumors had targetable alterations, only a small number of cases were able to access appropriate therapies due to availability and access issues.

High drug prices, lack of insurance coverage, and systemic inefficiencies further limit the practical application of precision oncology. In many LMICs, targeted therapies

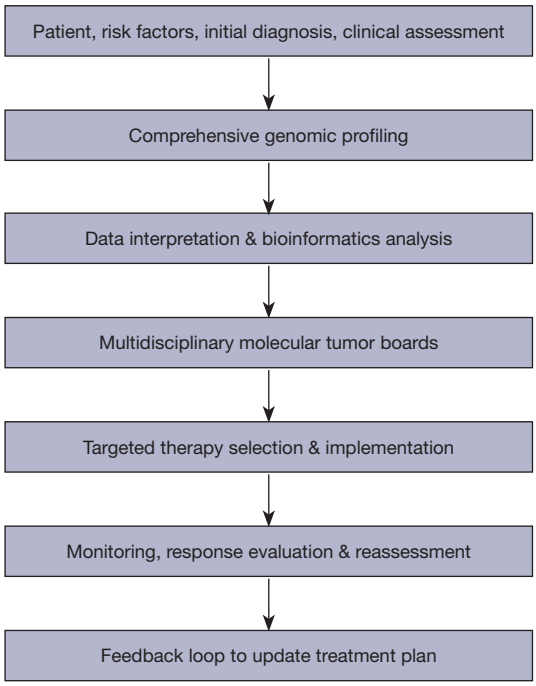

Figure 4 Conceptual model for personalized cancer therapy. The proposed conceptual framework for personalized cancer care starts with the patient undergoing standard diagnostics, including clinical assessment, imaging, and histopathological confirmation, before moving on to comprehensive genomic profiling. This step involves testing of the tumor (and germline of necessary) using targeted sequencing panels, whole exome or whole genome sequencing, or ctDNA analysis to capture actionable mutations. Subsequently, data interpretation and bioinformatic analysis using robust computational pipelines, AI-driven tools, and curated databases are used to highlight clinically significant genomic variation. These findings are then evaluated by a multidisciplinary MTB, where oncologists, pathologists, geneticists, bioinformaticians, and other specialists interpret the results within the patient's overall clinical context. This phase results in the selection and implementation of a targeted therapy. Such treatment plans are continually optimized through monitoring, response assessment and re-evaluation, integrating imaging, biomarker monitoring, and, where indicated, repeat genomic profiling to detect emerging resistance. A final feedback loop then refines the therapy, incorporating new data, clinical trial updates, and patient-specific factors for iterative improvement. AI, artificial intelligence; ctDNA, circulating tumor DNA; MTB, molecular tumor board.

remain prohibitively expensive, and healthcare systems lack the capacity to support advanced diagnostics. Even where therapies exist, regulatory restrictions and fragmented care models often delay or prevent their use. Addressing these barriers will require comprehensive policy reforms, tiered pricing strategies, and global health initiatives aimed at expanding equitable access.

To improve the clinical utility of genomic profiling, more integrated approaches are needed. The use of molecular tumor boards (MTBs) has shown promise in supporting personalized treatment decisions. For instance, Canino *et al.* (31) reported that NGS influenced therapy decisions in 9% of metastatic breast cancer cases. Expanding real-time genomic profiling in clinical trials can also help validate emerging biomarkers and inform treatment pathways.

Moreover, multi-omic approaches that integrate genomic, transcriptomic, and proteomic data are poised to refine precision oncology further. Pleasance *et al.* (21) demonstrated that combining RNA and DNA data enhances treatment selection, supporting a shift toward broader molecular characterization. However, realizing the full benefits of these advances will require coordinated efforts to address systemic barriers through targeted clinical training, patient education, standardized workflows, and supportive policy frameworks ensuring equitable implementation of precision oncology.

Proposed conceptual model

To address these real-world limitations, we propose a conceptual model (*Figure 4*) that integrates advanced genomic technologies, collaborative expertise, and adaptive clinical workflows into a patient-centered framework for personalized oncology. This model emphasizes the seamless incorporation of CGP, sophisticated bioinformatics interpretation, and multidisciplinary decision-making to guide individualized treatment strategies.

The patient journey begins with a standard clinical workup, including imaging, risk assessment, and histopathological evaluation, followed by in-depth genomic testing—ranging from targeted panels to exome or whole-genome sequencing—to detect actionable molecular alterations. These data are processed through validated bioinformatics pipelines that prioritize clinically relevant mutations and potential therapeutic options.

A multidisciplinary MTB—including oncologists, pathologists, geneticists, bioinformaticians, and other relevant specialists—reviews the molecular findings in conjunction with the patient's clinical context to determine a personalized treatment plan. This plan is not static; it evolves through ongoing monitoring using imaging,

biomarkers, and repeat genomic testing such as ctDNA, allowing real-time adaptation of therapy in response to treatment response or disease progression.

Based on this model, the proposed clinical guidelines highlight key implementation steps: clearly defined eligibility criteria for genomic testing, robust informed consent procedures, and selection of appropriate sequencing platforms tailored to clinical need. Standardized bioinformatics workflows are essential to ensure reproducibility, accurate variant calling, and functional annotation (*Table 4*).

MTBs play a central role in interpreting complex genomic data and addressing ethical and legal issues such as incidental germline findings and patient data privacy. Therapeutic decisions prioritize FDA-approved targeted agents matched to the tumor's molecular profile, which may include combination therapies or investigational approaches, like CRISPR-based gene-editing strategies, especially in cases of acquired resistance.

Regular outcome assessment through imaging, molecular biomarkers, and adaptive treatment adjustments ensures that care remains responsive to each patient's evolving disease trajectory. The model also emphasizes the importance of healthcare infrastructure, ongoing training for clinical staff, and policy development to support equitable access to genomic testing and the appropriate use of AI-driven decision-support systems.

In summary, this conceptual framework offers a practical, iterative approach to precision oncology by connecting cutting-edge genomic science with real-world clinical application. By placing the patient at the center of an integrated, data-driven ecosystem, it aims to maximize therapeutic efficacy, support dynamic care planning, and promote equitable implementation of personalized cancer treatment worldwide.

Discussion

Key findings

The conceptual model proposed in this review underscores the significance of integrating genomic insights, real-time data analytics, and multidisciplinary care into a cohesive framework for personalized oncology. Two transformative technologies, CRISPR gene editing and AI, are leading the way in this innovation, each making unique contributions to the advancement of cancer care. These technologies not only support but also enhance the fundamental pillars of the personalized oncology model, providing new opportunities to enhance diagnostic accuracy, therapeutic precision, and clinical outcomes.

CRISPR technology and gene editing in personalized cancer therapy

CRISPR technology and gene editing have revolutionized personalized medicine, especially in cancer treatment (95). By allowing precise editing of specific genetic sequences involved in tumorigenesis, CRISPR enables researchers and clinicians to create targeted therapies tailored to an individual's unique mutational profile. This capability represents a significant departure from traditional "one-size-fits-all" treatments, which are often associated with limited efficacy and adverse effects, and towards more refined, mutation-specific interventions (96,97).

CRISPR-Cas9, a widely used gene-editing system, uses RNA-guided endonucleases to introduce double-strand breaks at specific genomic locations (*Figure 5*) (95). These breaks activate the cell's natural repair mechanisms, allowing for either gene disruption or the insertion of desired genetic material. This precision editing opens the door for innovative therapeutic approaches, such as silencing oncogenes or reactivating tumor suppressor genes, with a level of specificity that surpasses pervious gene-editing tools.

A significant application of CRISPR technology lies in its potential for screening and correcting mutations that drive cancer development (98). Many cancers are fueled by specific genetic aberrations that confer growth advantages. Preclinical studies have demonstrated the feasibility of correcting such mutations in genes like TP53, PTEN, KRAS, and ARID1A using CRISPR-Cas9 systems, restoring their tumor-suppressive functions or altering oncogenic signaling pathways (99,100).

CRISPR also enables combinatorial targeting of multiple genes within a signaling network, addressing the complexity of cancer biology and drug resistance (98). By designing multiplexed CRISPR strategies, researchers can disrupt several genes simultaneously, which may help overcome tumor heterogeneity and reduce the likelihood of therapeutic escape mechanisms.

A pivotal moment in the evolution of genome editing was recently marked by regulatory approval. In 2023, the FDA approved CASGEVY™, the first CRISPR/Cas9-based gene therapy. This marks a major milestone in clinical gene editing. CASGEVY is a one-time, cell-based therapy for patients aged 12 years and older with sickle cell disease

Table 4 Proposed conceptual model with clinical practice guidelines for integrating and fostering personalized medicine in oncology

Steps	Descriptions
Patient evaluation and genomic testing	
Eligibility criteria	Consider comprehensive genomic testing for patients diagnosed with advanced, metastatic, or refractory cancers, or those with early-stage cancers where targeted therapies may improve outcomes. For certain tumor types (e.g., NSCLC, breast cancer, colorectal cancer, melanoma), strongly recommend genomic testing to identify driver mutations (e.g., EGFR, HER2, KRAS, BRAF). Include germline testing if there is a strong family history or suspicion of hereditary cancer syndromes (e.g., BRCA1/BRCA2)
Informed consent	Clearly explain the benefits and limitations (e.g., false negatives, uncertain variants, cost) of genomic testing. Discuss potential incidental germline findings and how they may affect family members
Choice of test	Targeted gene panels allow rapid, cost-effective method when specific mutations are strongly suspected. Whole exome or whole genome sequencing offers broad coverage, particularly useful for complex cases or when partial testing is inconclusive. Liquid biopsy (ctDNA) should be considered when tissue biopsy is not feasible or to monitor minimal residual disease and emerging resistance
Data analysis and bioinformatics	
Standardized workflows	Adopt validated pipelines for read alignment, variant calling, and annotation (e.g., GATK, COSMIC, ClinVar). Integrate RNA expression profiling when feasible to refine interpretation for novel target discovery
Multidisciplinary interpretation	Ensure that bioinformaticians, molecular biologists, and clinicians work together to validate mutations of VUS, integrate functional predictions, and produce comprehensive reports
AI and machine learning deployment	Use AI/ML algorithms to prioritize variants, predict drug response, or classify tumor subtypes. Validate predictions with established clinical and laboratory tests before making final treatment decisions
MTB review	
Regular case discussions	Convene an MTB to discuss comprehensive genomic profiles in light of each patient's clinical presentation. Collaborate with medical oncologists, pathologists, radiologists, palliative care experts, and genetic counselors as needed
Ethical considerations	Be transparent about how decisions are made, including how to deal with incidental findings or lack of data on certain variants. Discuss data privacy, especially if sharing genomic data across research networks
Decision support	Incorporate clinical decision support tools (e.g., OncoKB, CIViC, or local validated databases) to link detected mutations with potential therapeutic targets, investigational drugs, or clinical trials
Targeted therapy and combination treatments	
Drug selection	Prioritize FDA-approved therapies that match to the patient's actionable mutations, taking into account safety, patient preference, and comorbidities. If no standard targeted agent is available, consider investigational options through clinical trials
Combination therapy	Evaluate synergies using AI-driven or evidence-based prediction models to overcome eventual resistance (e.g., EGFR inhibitors plus anti-angiogenic drugs). Avoid overlapping toxicities by careful dosing and close monitoring of adverse events
CRISPR gene-editing approaches (investigational)	If available, consider for refractory cases and ensure robust informed consent detailing potential risks and benefits of a research protocol
Monitoring, outcome evaluation, and follow-up	
Assessment frequency	Base imaging, biomarker testing, and genomic re-analysis on tumor type and treatment regimen (e.g., every 6–12 weeks). Use ctDNA to detect early molecular progression or the emergence of resistance
Adaptive treatment strategies	At signs of progression or unacceptable toxicity, re-biopsy or perform repeat genomic/concomitant transcriptomic testing to understand new resistance mechanisms. Escalate treatment to novel agents, combination regimens, or metabolic therapies
Data sharing and reanalysis	Encourage data sharing (in accordance with privacy and national regulations) to improve variant classification over time. Regularly re-examine previously inconclusive or "unknown significance" variants against updated databases

Table 4 (*continued*)

Table 4 (*continued*)

Steps	Descriptions
Infrastructure, training, and policy considerations	
Clinical infrastructure	Establish specialized centers with access to high-throughput sequencing technologies and in-house or collaborative expert bioinformatics support
Healthcare professional education	Provide ongoing training for oncologists, pathologists, genetic counselors, nurses, and allied staff in the interpreting genomic data and communication of results to patients
Equity and accessibility	Advocate for insurance coverage or national programs to subsidize genomic diagnostics, particularly in underserved or low-income areas. Facilitate telemedicine or remote consultation service to widen patient access to specialized expertise.
Regulation and ethics	Develop clear guidelines for the use of AI in patient care, focusing on transparency, bias mitigation, and safety. Promote the responsible use of patient genomic data, respecting privacy regulations (e.g., GDPR in Europe, HIPAA in the US) and the ethical principles of beneficence, autonomy, and justice
Anticipated benefits and future directions	
Enhanced treatment efficacy	Personalized selection of targeted agents can improve response rates and overall survival in various solid and hematologic malignancies
Reduced toxicity	By targeting treatments to specific molecular alterations, potential off-target side effects can be minimized
Rapid innovation	The integration of emerging technologies (e.g., CRISPR, advanced AI/ML) is opening new avenues for real-time re-stratification and next-generation drug development
Increased collaboration	The continued expansion of public/private databases and multi-institutional studies promotes a global approach to refining guidelines, especially for rare mutations
Iterative improvement	As more data accumulates, guidelines and best practices will evolve, continuously improving precision cancer care through an adaptive learning healthcare system

AI, artificial intelligence; BRAF, v-Raf murine sarcoma viral oncogene homolog B; CRISPR, clustered regularly interspaced short palindromic repeats; ctDNA, circulating tumor DNA; EGFR, epidermal growth factor receptor; FDA, Food and Drug Administration; GDPR, General Data Protection Regulation; HER2, human epidermal growth factor receptor 2; HIPAA, Health Insurance Portability and Accountability Act; KRAS, Kirsten rat sarcoma viral oncogene homolog; ML, machine learning; MTB, molecular tumor board; NSCLC, non-small cell lung cancer; VUS, variants of uncertain significance.

and recurrent vaso-occlusive crises (101). The treatment involves editing the patient's hematopoietic stem cells to reduce the expression of the BCL11A gene, a repressor of γ-globin. This results in increased fetal hemoglobin production, effectively mitigating disease symptoms (102). The success of CASGEVY™ demonstrates the therapeutic viability of CRISPR-Cas9 and is likely to inspire future gene-editing-based treatments for other genetic diseases, including many forms of cancer.

In addition to correcting mutations, CRISPR technology is actively being explored to enhance immunotherapy, a transformative field in cancer treatment. While immune checkpoint inhibitors have shown remarkable efficacy against certain malignancies (103), responses can be inconsistent due to variability within tumor microenvironments. Researchers are investigating how they can use CRISPR tools not only to enhance anti-tumor immunity but also engineer immune cells (e.g., T-cells) so they better recognize and eliminate malignant cells based on their unique genetic signatures (104).

One example is chimeric antigen receptor (CAR)-T cell therapy, where a patient's T-cells are modified *ex vivo* using viral vectors to target tumor-specific antigens like CD19, found in B-cell malignancies such as acute lymphoblastic leukemia (ALL) (105,106). However, the use of viral vectors carries risks of off-target effects and presents logistical challenges in clinical production (107). CRISPR/Cas9 offers a more precise and scalable alternative, potentially increasing safety and expanding applicability across a wider range of solid and hematologic tumors.

Despite the remarkable progress, challenges remain. Ethical concerns surrounding human genome manipulating must be addressed within robust regulatory frameworks before clinical implementation (108). Equitable access to

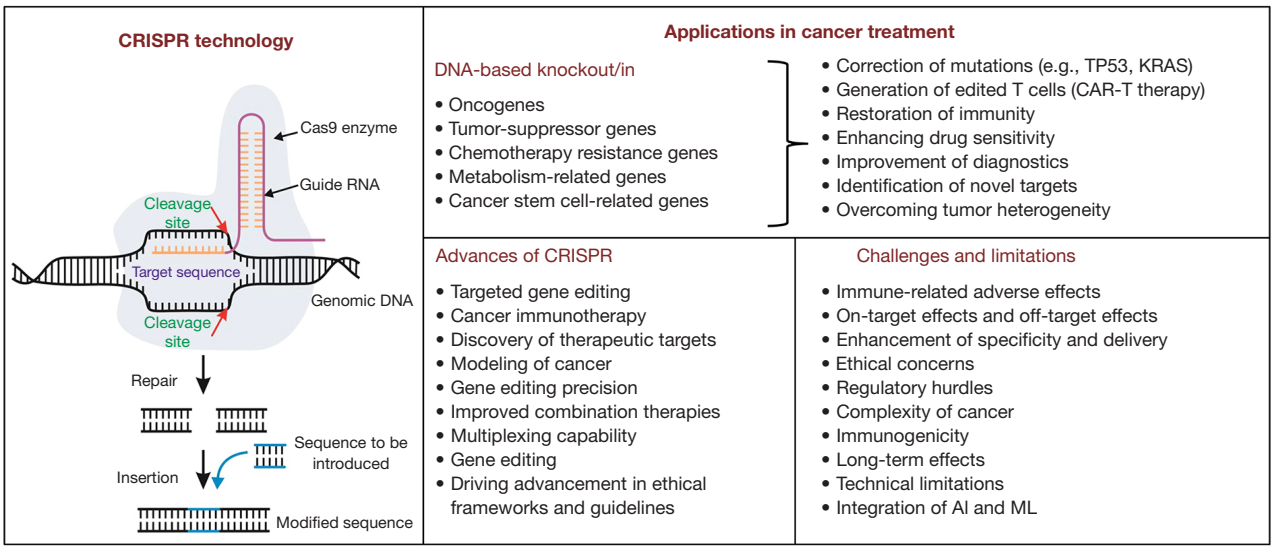

Figure 5 Overview of CRISPR technology in personalized medicine for cancer treatment. This figure explains the mechanism, applications, advances, challenges, and limitations of CRISPR/Cas9 technology in personalized cancer therapies. The left section illustrates the CRISPR technology, showing how RNA-guided endonucleases bind to specific DNA sequences, create double-strand breaks, and facilitate gene editing through the cell's natural repair processes. Applications in cancer treatment include correcting oncogenic mutations (e.g., TP53, KRAS), enhancing immune responses with engineered T-cells for CAR-T therapy, and using multiplexed targeting strategies to address tumor heterogeneity. CRISPR technology offers advantages over traditional methods for improving personalized medicine, but also presents challenges and limitations that may be addressed through integration of AI and ML to analyze large genomic data sets and predict patient outcomes. AI, artificial intelligence; CAR, chimeric antigen receptor; CRISPR, clustered regularly interspaced short palindromic repeats; ML, machine learning.

CRISPR-based therapies and diverse representation in clinical trials are also critical to ensure that innovations benefit all populations.

Another area requiring continued focus is the safe and efficient delivery of CRISPR components to target tissues or cells without affecting healthy adjacent tissue. Current delivery methods, such as liposomes, nanoparticles, and plasmid DNA constructs, rely heavily on traditional transfection techniques, which may be inadequate given biological complexities (95). Future advancements may stem from integrating emerging technologies like nanotechnology, biomaterials, and principles from synthetic biology, aimed at optimizing targeting efficiency while minimizing off-target effects and unintended consequences (95,109).

In conclusion, the convergence of genome editing, biotechnology, and personalized medicine principles is reshaping the future of cancer care. Tools like CRISPR not only provide unmatched precision in modifying disease-driving genes but also support broader strategies involving immune modulation and combination therapies. The approval of CASGEVY™, the first CRISPR therapy, illustrates that we are entering a new era where gene editing can revolutionize treatment approaches. Despite ongoing challenges related to ethics, access, safety, and clinical translation, continued interdisciplinary collaboration will be crucial in realizing the full potential of CRISPR-based personalized therapies and enhancing outcomes for cancer patients globally.

Artificial intelligence (AI) and ML in personalized cancer therapy

The integration of AI and ML into personalized medicine is rapidly transforming treatment selection in cancer care (110). As the volume of genomic and clinical data continues to grow, AI algorithms offer a powerful means of extracting meaningful patterns and insights that may be difficult or impossible for human researchers to discern (47). By leveraging predictive analytics, AI can assist clinicians in identifying the most effective, individualized treatment

options based on a patient's unique genetic profile, tumor characteristics, and clinical history.

One of the most significant advantages of AI and ML lies in their capacity to process and analyze vast, heterogeneous datasets at unprecedented speed and scale (47). Cancer research generates diverse data types, including genomic and transcriptomic sequences, proteomic signatures, clinical trial outcomes, imaging data, and demographic information. Advanced AI techniques are capable of integrating and analyzing this multimodal data to provide a more holistic understanding of each patient's condition.

Moreover, AI-driven platforms are revolutionizing biomarker discovery, a critical step in developing targeted therapies (111). ML algorithms can sift through large-scale datasets, derived from clinical trials, biobanks, or real-world evidence, to identify novel biomarkers associated with specific cancer subtypes or therapeutic responses. These insights enable clinicians to stratify patients more precisely and select therapies with higher probabilities of success based on individual molecular features.

Another exciting application of AL in oncology is in the optimizing combination therapies (49), a strategy commonly employed to overcome tumor resistance. AI models trained on historical treatment outcomes can predict synergistic interactions between therapeutic agents, allowing the development of personalized drug regimens that maximize efficacy while minimizing toxicity. In addition, AI-powered survival analysis models are being used to predict patient outcomes by incorporating factors such as genetic mutations, treatment history, comorbidities, and demographic variables (112). These tools support risk stratification and aid in tailoring treatment intensity, surveillance strategies, and follow-up care to patient-specific prognostic profiles.

Despite the clear potential benefits of AI and ML, several challenges must be addressed to facilitate seamless integration into existing workflows. Issues related to data interoperability, standardization, and system compatibility must be overcome to ensure the reliability and scalability of AI applications in healthcare settings (113,114). Equally important are concerns surrounding data privacy and cybersecurity, given the sensitive nature of genomic and health-related information. Adherence to stringent regulatory frameworks is essential to protect patient confidentiality while enabling responsible data sharing for innovation.

As discussed, ethical implications of AI applications in clinical decision-making require ongoing scrutiny. Transparency and accountability in algorithmic predictions are crucial for building trust among patients and providers. Ensuring fairness and mitigating biases within AI models are necessary to prevent disparities in care and to promote equitable access to advanced technologies.

As AI continues to evolve, interdisciplinary collaboration is vital for ensuring its responsible and effective application (115,116). Engaging experts from diverse fields, including bioinformatics, oncology, computational biology, ethics, law, and patient advocacy, can guide the development of AI solutions that are both scientifically sound and socially responsible. Incorporating stakeholder feedback throughout the design and implementation process also fosters the creation of user-friendly, accessible interfaces that promote adoption across varied clinical settings.

In conclusion, the convergence of AI and ML with advances in genomics and biotechnology heralds a new era of personalized cancer therapy. Intelligent systems are poised to enhance decision-making, improve treatment precision, and significantly extend survival rates by aligning therapeutic strategies with individual patient needs. As these technologies mature, ensuring ethical, equitable, and interdisciplinary integration will be key to realizing their full potential in transforming cancer care worldwide.

Strengths and limitations

This review highlights significant advancements in personalized medicine, particularly in the context of cancer treatment, by synthesizing current knowledge on genomic profiling and targeted therapies. Its strengths lie in the comprehensive overview of emerging technologies such as CRISPR and AI, which are reshaping treatment paradigms and enhancing the precision of therapeutic strategies. However, limitations include the potential for selection bias in included studies and the challenge of generalizing findings across diverse patient populations due to variations in access to genomic testing and targeted therapies. Additionally, while the review discusses technological innovations, it may not fully address the ethical implications and practical challenges associated with implementing these advancements in clinical practice. Finally, economic aspects are not discussed which might be a limitation, specifically in low-income countries.

Comparison with similar research

Several recent reviews have documented significant

advancements in personalized medicine within oncology (117-120). Building upon this growing body of literature, our scoping review offers a comprehensive and up-to-date synthesis of recent innovations, with a particular emphasis on advances in genomic profiling and targeted therapies for cancer treatment.

What distinguishes our review from previous works is its holistic approach, which not only synthesizes established practices but also integrates insights from emerging technologies that are shaping the future of precision oncology. Specifically, we highlight the transformative roles of CRISPR gene editing and AI, exploring how these innovations are being incorporated into clinical decision-making to support more accurate, individualized treatment strategies.

Our analysis further addresses critical implementation challenges, including issues related to data interpretation, accessibility, and integration into routine clinical workflows, areas that are often underrepresented in prior reviews. By contextualizing these barriers within the broader framework of precision oncology, we provide practical insights that may inform future research, policy development, and clinical application.

Moreover, our review introduces an up-to-date conceptual model and practice-oriented recommendations for integrating personalized medicine into oncology care. This framework is designed to guide clinicians, researchers, and healthcare systems in navigating the complexities of translating genomic insights into actionable, patient-centered therapies.

Explanations of findings

The findings of this review emphasize the transformative impact of genomic profiling on personalized medicine, particularly in cancer treatment. By identifying specific genetic alterations that drive tumor growth, clinicians can tailor targeted therapies for individual patients, enhancing treatment effectiveness and overall outcomes. For example, identifying actionable mutations like EGFR or BRAF alterations allows the selection of treatments that target the molecular pathways involved in cancer progression. Additionally, advancements in technologies such as NGS have significantly improved our ability to conduct comprehensive genomic analyses, providing deeper insights into tumor heterogeneity and resistance mechanisms. The integration of AI and ML into bioinformatics further enhances this process by enabling more accurate interpretation of complex genomic data and facilitating optimal treatment selection based on patient-specific profiles. Together, these points illustrate how leveraging genomic insights not only guides clinical decision-making but also paves the way for innovative therapeutic strategies that show promise for enhancing patient care in oncology moving forward.

Implications and actions needed

The implications of this review are profound, as they highlight the necessity for a paradigm shift in cancer treatment towards a more personalized approach rooted in genomic insights. To fully realize the potential of personalized medicine, several actions are needed. First, there must be an increased emphasis on expanding access to genomic testing and targeted therapies across diverse populations to ensure equitable healthcare delivery. This includes addressing barriers such as cost, availability of testing facilities, and training for healthcare professionals in interpreting genomic data effectively. Additionally, fostering interdisciplinary collaboration among oncologists, geneticists, bioinformaticians, and policymakers is crucial to develop comprehensive frameworks that integrate genomic profiling into routine clinical practice. Furthermore, ongoing research should focus on refining bioinformatics tools and developing robust guidelines for the ethical application of emerging technologies like CRISPR and AI in patient care. By taking these steps, the medical community can enhance treatment personalization and improve outcomes for cancer patients globally.

Conclusions

Personalized medicine is transforming the field of oncology, with genomic profiling emerging as a key factor in customizing cancer treatments for individual patients. The integration of advanced technologies like NGS, CRISPR-based gene editing, and AI has sped up the progress of identifying actionable mutations, predicting treatment outcomes, and creating more precise therapeutic regimens. However, despite these advancements, the path to fully integrated precision oncology remains intricate. Looking forward, a practical vision for personalized cancer care involves tackling various crucial challenges. These challenges include ensuring fair access to genomic testing, improving healthcare infrastructure, enhancing clinician education, and establishing solid ethical and regulatory

frameworks to govern the use of genomic data. Moreover, the transition of research breakthroughs into everyday clinical practice requires collaboration across disciplines, consistent funding, and strategies that prioritize the need of patients. To truly redefine oncology care, future initiatives must prioritize not only innovation but also inclusivity, scalability, and sustainability. Personalized medicine will not be a one-size-fits-all solution; it will require flexible models that can adapt alongside scientific advancements and healthcare system capabilities. By aligning technological progress with practical and ethical considerations, we can move closer to a future where cancer treatment is not only more effective, but also more equitable, accessible, and responsive to the diverse needs of patients worldwide.

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Footnote

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