

## Personalized Treatment in Oncological Therapeutics: Unlocking Targeted Cancer Treatment

**Mufakkir Aziz<sup>1, 2</sup>, Muhammad Asif<sup>1</sup>, Inayat Ullah<sup>3</sup>, Umme Salma<sup>4</sup>, Nabeela Tabassum Sial<sup>5</sup>, Sumbul Qamar<sup>6</sup>, Aamna Shah<sup>7\*</sup>, Salwa M.A. Dahesh<sup>8</sup>**

<sup>1</sup>Institute of Microbiology, Gomal University, Dera Ismail Khan.

[asifmatrah9876@gmail.com](mailto:asifmatrah9876@gmail.com)

<sup>2</sup>Department of Pathology, Brigadier Shafiq Ahmad Niazi Memorial Trust Hospital Bhakkar.

[mufakkiraziz125@gmail.com](mailto:mufakkiraziz125@gmail.com)

<sup>3</sup>Department of Health And Biological Sciences, Abasyn University Peshawar

[armaninayatullah@gmail.com](mailto:armaninayatullah@gmail.com)

<sup>4</sup>Department of Pharmacy, Sardar Bahadur Khan Women's University, Quetta, Baluchistan, Pakistan

[Sam\\_Us19@yahoo.com](mailto:Sam_Us19@yahoo.com)

<sup>5</sup>Lahore College for Women University, Lahore, Punjab, Pakistan.

[nabeela.tabassum@lcwu.edu.pk](mailto:nabeela.tabassum@lcwu.edu.pk)

<sup>6</sup>Al Reziq College of Pharmacy, Sargodha.

[sumbul\\_pharmacist@hotmail.com](mailto:sumbul_pharmacist@hotmail.com)

<sup>7</sup>Department of Pharmacy, The University of Lahore, Sargodha Campus.

[aamna.shah@pharm.uol.edu.pk](mailto:aamna.shah@pharm.uol.edu.pk)

<sup>8</sup>Research Institute of Medical Entomology, the General Organization for Teaching Hospitals and Institutes, Giza, Egypt.  
[Salwamohamed970@gmail.com](mailto:Salwamohamed970@gmail.com)

### ABSTRACT

Personalized medicine has emerged as a transformative approach tailoring cancer therapeutics for individual patients, encompassing unique genetic, molecular, and clinical characteristics. Conventional "one-size-fits-all" treatments have endorsed more focused and precise approaches, with ultimate advancement in genomics, biomarker identification, and cutting-edge technologies, including artificial intelligence (AI), CRISPR gene editing, and nanoparticulate system approaches. Personalized therapeutic approaches, including genomic and molecular profiling, pharmacogenomics, epigenetic modulation, and immunotherapy, additionally address cost, tumor heterogeneity, and ethical concerns. Despite notable progression, tumor heterogeneity, complex/concomitant molecular modulations, along limited access to genomic diagnostics, suggested further refining of therapeutic assessments via CRISPR gene management and artificial intelligence. Furthermore, recent clinical studies and future directives provide possible suggestions regarding personalized medicines' potential for the establishment of a gold standard Oncological treatment with improved patient outcomes and revolutionized oncological management at dual clinical and systemic levels..

**Keywords:** Cancer, Treatment, Personalized Medicine, Oncology

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### 1. INTRODUCTION

Historically, cancer treatment consisted of three main modalities: surgery, chemotherapy, and radiation therapy. Surgery is frequently performed to treat circumscribed tumors, to completely remove malignant tissue. However, its efficacy is reduced in metastatic situations, where cancer cells have moved beyond the initial site.[1]. Chemotherapy uses cytotoxic

chemicals to target rapidly dividing cells, but its systemic nature frequently results in major side effects such as immunological suppression, gastrointestinal distress, and neuropathy.[2]. Similarly, radiation therapy uses high-energy ionizing radiation for damaging cancer cells; however, collateral damage to healthy tissues remains a problem, leading to consequences like fibrosis and secondary malignancies.[3].

Personalized medicine, often called precision oncology, transforms cancer treatment by customizing therapies based on the genetic, molecular, and epigenetic profiles of individual tumors. Advances in high-throughput genomic technologies, such as next-generation sequencing (NGS), have allowed for the detection of actionable genetic variants, opening the door for targeted medicines.[4]. Imatinib, a tyrosine kinase inhibitor that targets the BCR-ABL fusion protein in chronic myeloid leukemia, was a breakthrough in treatment outcomes.[4]. Similarly, HER2-targeted therapy in breast cancer and EGFR inhibitors in non-small cell lung cancer have significantly improved survival and quality of life.[5, 6].

Beyond targeted therapies, the personalized approach includes immunotherapies such as immune checkpoint inhibitors (e.g., pembrolizumab, nivolumab) and CAR-T therapy.[7]. These immunotherapies utilize the patient's immune system to fight cancer, with great specificity and durability.[8]. Personalized medicine, which aligns treatment techniques with each tumor's unique molecular landscape, not only enhances therapeutic efficacy but also minimizes side effects, signaling a dramatic break from the one-size-fits-all paradigm of standard cancer treatments.[8, 9].

This paper delves into the growing landscape of customized medicine in cancer treatment. It seeks to understand the integration of genetic profiles, targeted medicines, and immunotherapies into clinical practice, as well as the transformative influence they have on patient outcomes[4]. Furthermore, the study investigates the problems involved with adopting personalized medicine, such as high costs, limited access in resource-constrained countries, and ethical concerns about genetic data[10, 11]. Finally, it discusses future trends in precision oncology, emphasizing the potential of personalized medicine to overcome the constraints of traditional medicine and redefine the standard of care in cancer.

### Historical Perspective and Key Components of Personalized Medicine in Cancer Treatment

#### Traditional Cancer Therapies

Historically, cancer treatments were primarily "one-size-fits-all," aiming to target rapidly dividing cells regardless of specific patient differences. Conventional therapies such as chemotherapy, radiation, and surgery try to eradicate cancer cells in large numbers, often causing considerable collateral harm to healthy organs.[4]. These treatments were predicated on the premise that all cancer types within a given organ or tissue responded similarly to the same therapeutic method, regardless of genetic, molecular, or individual patient characteristics.[12]. As a result, these treatments frequently produced unsatisfactory results for patients, particularly those with distinct genetic profiles or variances in cancer risk. Furthermore, the toxicity of such treatments resulted in decreased quality of life and increased long-term adverse effects for many patients [13].

#### Genomic Profiling

Genomic profiling is the foundation of personalized medicine, allowing the discovery of genetic abnormalities, chromosomal rearrangements, and epigenetic changes that drive tumor growth and progression[5]. High-throughput technologies like next-generation sequencing (NGS) and whole-exome sequencing have transformed cancer diagnosis by identifying actionable targets. For instance, mutations in the EGFR gene in non-small cell lung cancer (NSCLC) or the BRAF V600E mutation in melanoma influence the choice of targeted therapy, like gefitinib or vemurafenib [5, 14].

Furthermore, genomic profiling helps in understanding tumor heterogeneity by revealing multiple subclonal populations inside a single tumor. This knowledge is critical for creating combination therapies to combat drug resistance[15]. Programs such as The Cancer Genome Atlas (TCGA) and the International Cancer Genome Consortium (ICGC) have given vital tools for mapping the genetic landscape of diverse malignancies, hence supporting progress in precision oncology[16].

#### Targeted therapies

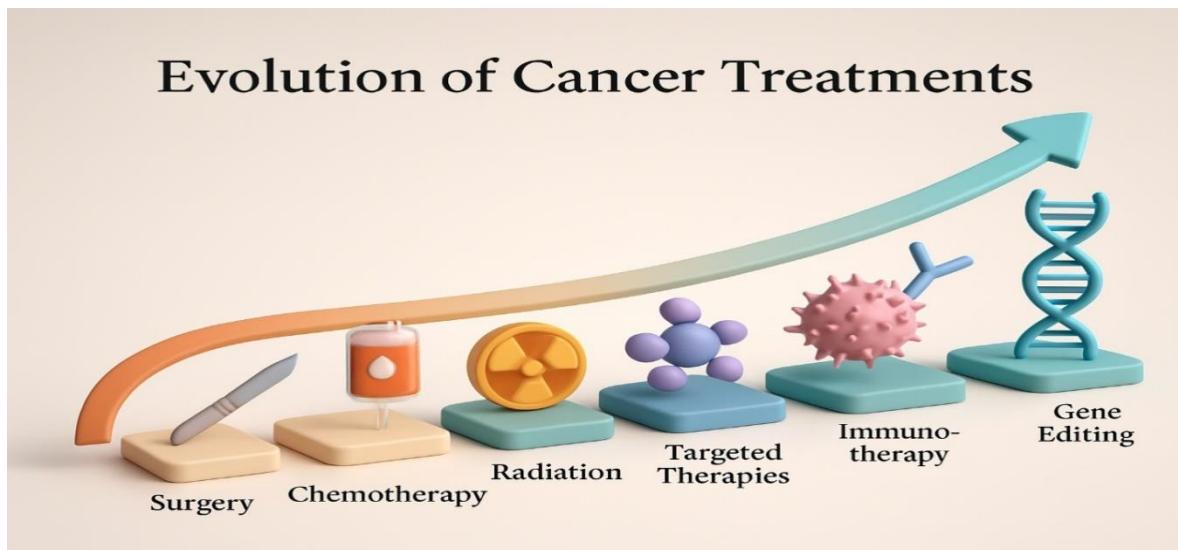
Targeted therapies take advantage of molecular defects unique to cancer cells, providing greater specificity and lower toxicity than standard chemotherapy. Tyrosine kinase inhibitors (TKIs) such as imatinib for chronic myeloid leukemia (CML) and trastuzumab for HER2-positive breast cancer demonstrate the efficacy of this strategy [17]. Beyond small-molecule inhibitors, monoclonal antibodies such as bevacizumab, which targets vascular endothelial growth factor (VEGF), restrict angiogenesis, depriving tumors of blood supply[18]. PARP inhibitors, such as Olaparib, which is utilized in BRCA-mutated ovarian and breast malignancies, demonstrate the importance of targeting DNA repair pathways to exploit tumor-specific vulnerabilities [19].

#### Immunotherapy

Immunotherapy is a revolutionary cancer treatment approach that uses the patient's immune system to battle tumors. Immune checkpoint inhibitors (ICIs) like pembrolizumab and nivolumab suppress inhibitory pathways such as PD-1/PD-L1 and CTLA-4, allowing T-cells to attack malignancies [20]. These medicines have demonstrated extraordinary success in melanoma, NSCLC, and other malignancies, frequently resulting in long-lasting responses. Another innovation is chimeric antigen receptor (CAR) T-cell therapy, which reprograms patients' T-cells to target and kill cancer cells.

Tisagenlecleucel, a CAR-T therapy demonstrating successful management of hematological malignancies such as acute lymphoblastic leukemia [8].

In addition to checkpoint inhibition and CAR-T treatment, cancer vaccinations and oncolytic viruses are developing immunotherapeutic approaches. Cancer vaccines seek to prime the immune system against tumor-specific antigens, whereas oncolytic viruses selectively infect and kill cancer cells, releasing tumor antigens that stimulate immune responses [8].



**Figure 1.** The historical evolution of cancer treatments from traditional methods like surgery and radiation to modern approaches, including targeted and precision therapies.

**Table 1: Comparative analysis of Traditional and Personalized Cancer treatments.**

Feature	Traditional Therapies (Surgery, Chemo, Radiation)	Personalized Medicine (Targeted, Immuno, Gene Editing)
<b>Approach</b>	One-size-fits-all; targets rapidly dividing cells	Tailored to individual genetic/molecular profiles
<b>Specificity</b>	Low; affects healthy cells	High; targets specific cancer pathways/markers
<b>Side Effects</b>	Significant (e.g., immunosuppression, neuropathy)	Generally reduced; more focused toxicity
<b>Efficacy</b>	Variable; limited in metastatic cases	Improved outcomes, especially for specific subtypes
<b>Examples</b>	Surgery, broad chemotherapy, and external beam radiation	Imatinib, Pembrolizumab, CAR-T therapy, CRISPR
<b>Underlying Principle</b>	Cytotoxic effects, physical removal	Molecular targeting, immune system modulation

### Importance of Targeted Approaches in Precision Medicine

Precision medicine enables oncologists to predict patients more accurately and is crucial in augmenting treatment plans, avoiding useless surgical procedures, and improving overall patient outcomes. Novel targeted treatment protocols provide

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advanced cancer treatment with the beneficial advantage of lower toxicity and improved treatment tactics[8].

By customizing treatments with respect to a response of a particular patient's profile, the incorporation of targeted techniques in precision medicine led to improved patient care. Targeted therapies exhibit the potential to revolutionize cancer treatment via improved patient outcomes through the development of scientific technologies[21]. The continued analysis and application of current innovative therapeutics against the management of complicated illnesses will ultimately result in efficacious cancer management in the near future. Precision medicine is vital regarding optimization of treatment techniques, thereby inhibiting the provision of unnecessary treatments, and ultimately improving patient care[22].

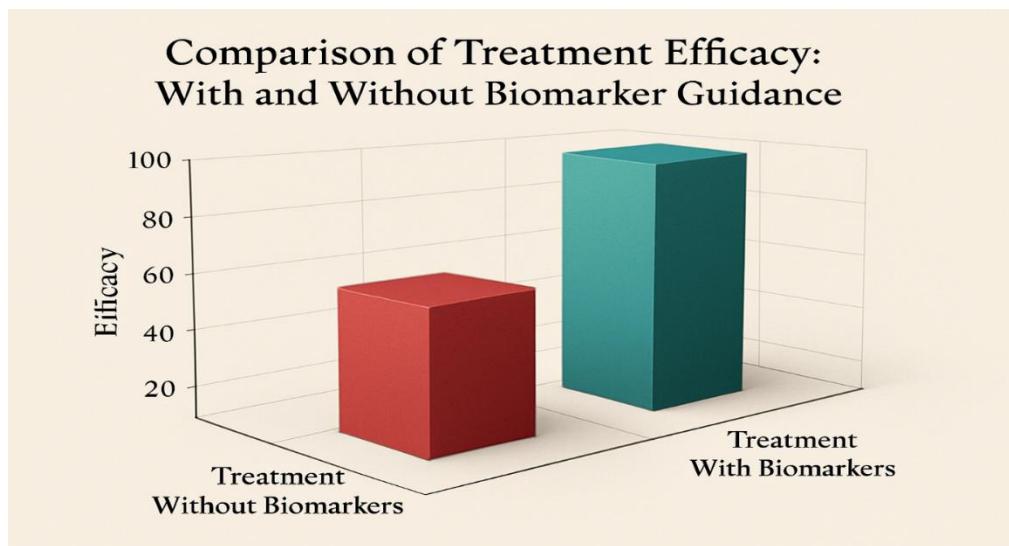
## Principles of Personalized Medicine in Cancer

### Genomic and Molecular Profiling

Genomic and molecular profiling are critical for understanding cancer's distinct genetic landscapes. Cancer cells' DNA, RNA, and protein levels can be analyzed to discover particular mutations, gene expressions, and molecular pathways that cause tumor progression. For example, next-generation sequencing (NGS) has transformed how oncologists approach cancer treatment by revealing actionable genetic alterations such as BRCA1/2 mutations in breast cancer or KRAS mutations in colorectal cancer [23]. Personalized treatment plans are then created by customizing medicines to the genetic signatures of specific cancers, which improves efficacy while lowering negative effects [24].

### Biomarkers

Biomarkers are critical for selecting appropriate medicines since they distinguish specific cancer subtypes and predict treatment responses. For example, HER2 (human epidermal growth factor receptor 2) is a well-known biomarker in breast cancer that guides the use of targeted medicines like trastuzumab (Herceptin)[25]. Similarly, EGFR (epidermal growth factor receptor) mutations influence the usage of EGFR inhibitors in non-small cell lung cancer (NSCLC), such as gefitinib and erlotinib. These biomarkers aid in stratifying patients into subgroups who are most likely to benefit from specific medicines, improving results and reducing wasteful treatments [25]. The development of companion diagnostics has increased the importance of predictive biomarkers. FoundationOne CDx tests several gene changes to guide the usage of targeted medicines such as EGFR inhibitors, ALK inhibitors, and others across diverse cancer types [26].



**Figure 2** Comparative analysis of treatment efficacy with and without biomarker-guided treatment protocols.

### Liquid biopsies

Liquid biopsies identify circulating tumor DNA (ctDNA) in blood samples, offering a minimally invasive alternative to standard tissue biopsies. This technique aids in monitoring disease progression, tracking mutations, and guiding medication modifications. For example, liquid biopsies are utilized to detect mutations in EGFR for lung cancer patients and BRAF for melanoma patients, allowing for real-time, patient-specific therapy adjustments [27, 28].

### Pharmacogenomics

Pharmacogenomics investigates how genetic variations influence individual medication reactions. Personalized medicine uses pharmacogenomic testing to anticipate how a patient's genetic profile affects drug metabolism, efficacy, and toxicity. Individual reactions to 5-fluorouracil, a chemotherapy medication used in colorectal cancer, are influenced by genetic

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variations in its metabolism; some people have significant toxicity, while others gain greatly from the treatment. Similarly, changes in genes such as UGT1A1 influence irinotecan metabolism, affecting its efficacy and safety[29, 30]. Pharmacogenomics improves cancer treatment precision by customizing drug regimens to each individual's genetic composition, resulting in improved efficacy and fewer adverse drug effects[31].

### Monitoring and Adaptive Treatment Strategies

Another important aspect of personalized medicine is the real-time monitoring of therapy responses using liquid biopsies and molecular imaging. Circulating tumor cells (CTCs) and ctDNA analysis can be used to assess minimal residual disease (MRD) and detect early relapse [32]. This enables clinicians to change treatment tactics, including second-line medicines or combination approaches to combat growing resistance. In addition, adaptive therapy options based on computer models and artificial intelligence are gaining traction. These models use multi-omics data to predict tumor behavior and optimize therapy sequences, ushering in a new age of precision oncology [28].

### Precision Therapeutics

Precision therapy is one of the most efficient uses of personalized medicine. Targeted treatments, such as vemurafenib for BRAF V600E-mutant melanoma and imatinib for chronic myeloid leukemia (CML), have altered the therapy landscape by reaching high specificity and efficacy [33]. Immunotherapies, such as immune checkpoint inhibitors and CAR-T treatments, use the patient's immune system to combat cancers with specific molecular signatures [22]. Personalized radiotherapy, which uses imaging biomarkers to characterize tumor features and improve radiation delivery, demonstrates how precision extends beyond pharmacological treatments. Stereotactic body radiation (SBRT) reduces damage to healthy tissues while accurately targeting cancer cells [34].

**Table 2: Key factors associated with the personalized medication system.**

Component	Description	Role in Personalized Medicine
<b>Genomic Profiling</b>	Analysis of DNA, RNA, and protein to identify genetic abnormalities	Foundation for identifying actionable targets and tailoring treatments
<b>Biomarkers</b>	Biological indicators that distinguish cancer subtypes and predict response	Guide selection of appropriate therapies (e.g., HER2, EGFR mutations)
<b>Liquid Biopsies</b>	Non-invasive detection of circulating tumor DNA (ctDNA) in blood	Real-time monitoring of disease, tracking mutations, guiding therapy
<b>Pharmacogenomics</b>	Study of how genetic variations influence individual drug responses	Predicts drug metabolism, efficacy, and toxicity; customizes drug regimens
<b>Immunotherapy</b>	Utilizes the patient's immune system to fight cancer	Enhances immune response against tumors (e.g., ICIs, CAR-T therapy)
<b>Targeted Therapies</b>	Drugs that specifically target molecular defects in cancer cells	Higher specificity and lower toxicity than traditional chemotherapy

### Targeted Therapies for Specific Cancer Types

#### Breast Cancer:

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Targeted therapies employed for breast cancer management aim to specifically target molecular alterations aggravating tumor growth, like human epidermal growth factor receptor 2 (HER2)-positive breast cancer be efficaciously managed using HER2-targeted therapies, including trastuzumab, pertuzumab, and ado-trastuzumab emtansine. Hormone receptor-responsive breast cancer malignancies can effectively be treated with hormonal therapies capable of blocking estrogen or progesterone receptors, including tamoxifen and aromatase inhibitors[35].

### Lung Cancer

Here, targeted therapy is aimed at interrupting specific genetic alterations effectively involved in the progression of lung cancer. EGFR inhibitors, including gefitinib and Osimertinib, presented improved advantages in non-small cell lung cancer (NSCLC), including cases with EGFR mutations, while ALK inhibitors such as Crizotinib and Alectinib have been particularly approved for use in patients presenting ALK gene alterations. ROS1 and BRAF inhibitors are also being developed as targeted treatments for lung therapeutics, particularly in specific patient subgroups[36, 37].

### Colorectal Cancer

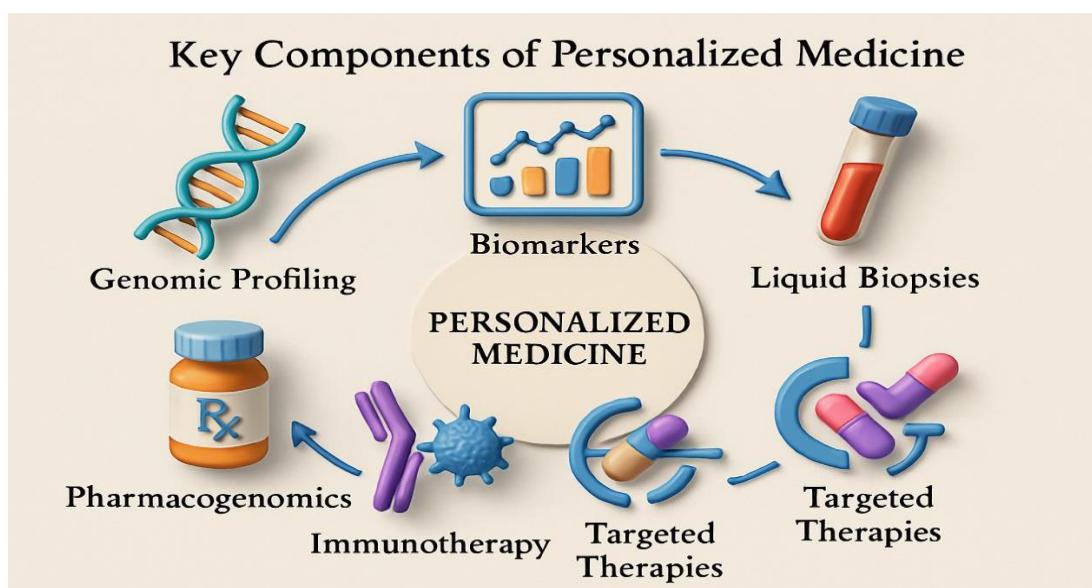
In colorectal cancer, targeted therapies mainly encompass inhibitory action on vascular endothelial growth factor (VEGF) and the epidermal growth factor receptor (EGFR) pathway. Bevacizumab is an antibody particularly effective against VEGF and exhibits the capability of blocking vascular growth. EGFR inhibitors, like cetuximab and panitumumab, block the EGFR pathway in KRAS wild-type colorectal cancer[38, 39].

### Melanoma

Targeted therapies for melanoma are particularly effective against the BRAF mutation, found to exist in approximately 50% melanomas. BRAF inhibitors, such as vemurafenib and dabrafenib, are medications that directly target altered BRAF proteins and ultimately block their activity; however, resistant cancer cells may ultimately be produced. The combination of BRAF inhibitors with MEK inhibitors such as trametinib is considered more effective[40, 41].

**Leukemias and Lymphomas:** Targeted therapies designed for leukemias and lymphomas include kinase inhibitors and monoclonal antibodies. The anti-CD20 antibody (rituximab) is efficaciously used for the treatment of chronic lymphocytic leukemia (CLL), whereas B-cell 179 is used in conjunction with chemotherapy for lymphomas. Tyrosine kinase inhibitors such as dasatinib, nilotinib, and imatinib are designed to target the BCR-ABL fusion gene in the case of chronic myeloid leukemia (CML)[42, 43].

Targeted treatment for specific cancer types has revolutionized cancer treatment via the successful management of precise molecular targets, thereby enhancing patient outcomes and reducing possible adverse effects. From research advancements, there is requisite for more targeted therapies leading to better treatment options and improved survival rates[44, 45].



**Figure 3** Key factors associated with personalized medications include genomic profiling, targeted, and immune therapies.

### Rationale of Nanobiotechnology

### The Remarkable Potential of Nanoparticles and Nanostructures in Biomedicine

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Nanoparticles (NPs) and other nanostructured materials, based on their minute size (1–100 nm), exhibit the unique capability of permeating cell membranes and interacting with internal organelles that ultimately trigger particular physiological processes[41]. Nanostructured substances based on inherent characteristics are a vital component of numerous biomedical applications, including sophisticated imaging technologies, drug delivery systems, contrast imaging agents and photothermal therapies[46].

### Precision Targeting for Cancer Therapeutics

When considering cancer theranostics (diagnosis and treatment), nanoparticles offer an essential benefit in comparison to traditional methods. These benefits arise from remarkable precision where NPs target specific tumor cells or tissues, thereby avoiding their metastasis to other nearby healthy tissues. The targeting process includes dual active and passive targeting mechanisms[47]. Passive targeting exploits the enhanced permeability and retention (EPR) effect, a unique characteristic of tumor tissues. Nanoparticles exhibit a unique potential of concentrating nanoparticles associated with leaky vasculature and the poor lymphatic drainage system of tumor cells[48].

Current drug delivery system augments therapeutic precision medication systems via the accumulation of nanoparticles precisely within tumor cells, thereby reducing toxicity to healthy tissues and overall improving treatment efficacy[48, 49].

In contrast, active targeting implicates functionalization of nanoparticles using particular ligands or antibodies that identify and recognize particular receptors overexpressed in cancer cells. These ligands might be tiny components with a strong affinity for target receptors, proteins, peptides, or aptamers [50, 51].

After binding, the nanoparticles either bind with the cell surface to deliver therapeutic medicament or imaging probes, or are taken up by cancer cells via receptor-mediated endocytosis. After appropriate accumulation of nanoparticles specifically in tumor cells, their therapeutic or diagnostic function specifically in cancer cells is noticed, which ultimately improves targeted drug delivery, reducing harm to healthy cells or tissues and improving therapeutic efficacy[52]. Unlike conventional diffusing medicaments, specifically engineered targeted NPs are designed to ultimately reach their intended destination. The current targeted system ultimately minimizes the risk of unfavorable side effects and cytotoxicity to normal healthy cells, most frequently encountered from non-specific targeting. Furthermore, targeted medication system also enhances therapeutic effectiveness with ultimate enhancement of therapeutic effectiveness and reduction of adverse effects, and improved patient compliance[53].

### 2.3. Revealing Cellular Processes and Identifying Biomarkers

Nanobiotechnology offers a robust framework of understanding intricate biological processes, signaling pathways, and disease progression offered by improving the effectiveness of new biomarker identification and exposing the mechanisms of therapeutic effectiveness, where nanobiotechnology greatly enhances our understanding of numerous malignancies [54]. Upon successful modification and functionalization of nanomaterials, researchers may augment their control over nanotechnology by combining numerous bioactive components like nucleic acids, medicinal ingredients, photosensitizers, and enzymes with nanoparticles. These mixtures in conjunction with particular biomaterials, are tailored to fulfill particular therapeutic requirements [55]. Currently, nanotechnology has provoked remarkable improvements in the areas of antimicrobial medicaments, cancer treatment/prevention, and the prevention of other related disorders [56].

### Emerging Frontiers in Nanomedicine:

Drug delivery technology has undergone an outstanding transformation via the development of nanoparticulate technology. Diverse nanocarriers exhibiting exceptional attributes and capabilities present hitherto unexploited possibilities for the targeted/controlled delivery of therapeutic components[57]. It provided open door for the development of novel therapeutic approaches regarding the precise and controlled release of medicinal components, e.g. development of innovative treatments presenting more efficacy with fewer adverse effects.

### Dendrimers

These meticulously engineered monodispersed macromolecules exhibit a compact core efficaciously covered with different functional groups. This architecture allowed maximal drug loading and controlled release, making dendrimers an ideal candidate for delivering anticancer drugs, imaging probes, and gene therapy vectors. Their homogeneity and enhanced cellular penetration based on their nanoscale size further enhanced their effectiveness regarding targeted drug delivery applications[58, 59].

The current therapeutic system allows maximum drug loading and controlled release, thereby making them an ideal candidate for delivering anticancer medicaments, imaging probes, and genetic therapy vectors. Their homogeneity, improved cellular uptake, and nanoscale size thereby enhance the therapeutic effectiveness by targeting cancer cells[59].

**Hollow caged carbon allotropes** provide a distinctive platform for entrapping medicaments and their subsequent release. Their functionalized surfaces might be targeted to deliver their reactions to certain stimuli, including changes in pH or light

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exposure can be used to initiate drug delivery[60]. Their ideal characteristics of delivering anticancer drugs, antibiotics, and imaging agents make them ideal in this regard.

**Nanobodies/Single-domain fragmented antibodies** and nanobodies are better soluble, stable, and tissue penetrating in comparison to their traditional counterparts, resulting in enhanced tumor targeting or penetration, making them an ideal drug delivery system[61]. Moreover, they may easily conjugate with other drugs or biomolecules, making them ideal multifunctional nanocarriers for theranostics, high-quality imaging, for anticancer treatment[62].

### Micelles

**Micelles**, i.e., Dynamic self-assembled arrangements of the amphiphilic block copolymers, exhibit a hydrophilic head and hydrophobic core. Current orientation allowed efficient encapsulation of dual hydrophobic and hydrophilic drugs, thereby enabling these moieties as a versatile drug delivery system. Moreover, their prolonged circulation and phagocytosis resistance resulted in enhanced therapeutic effectiveness[63, 64].

**Polymer-Drug Conjugates** are developed via covalent attachment of drugs to polymer chains, resulting in the formation of one product with augmented characteristics. The current method improves drug stability, solubility, and retention rate in the body, together with controlled release of the targeted drug to the targeted areas of disease in the body. In addition, the possibility of creating polymer-drug conjugates to be released by something more effectively enhances the therapeutic potential and reduces the systemic level side effects[65].

**Virus-like Particles (VLPs) and Caged Proteins (CPs)** are biomimetic nanocarriers that effectively mimic viral structures without viral genomics. VLPs and CPs offer inherent biocompatibility and reduced immune response risk, making them an attractive candidate for drug delivery systems, particularly for the management of cancer therapy. Additionally, their capability to provoke immune responses holds promising outcomes for vaccine synthesis and cancer immunotherapy[66].

**Biocompatible and versatile Self-Assembled Protein Nanoparticles** are derived from numerous proteins, including albumin, collagen, and soy. The inherent biodegradability and assistance of functionalization provoked versatile applications such as wound healing, tissue regeneration and drug delivery. Notably, albumin-based nanoparticulate system including Abraxane exhibit potential of carrying paclitaxel for cancer management, including virus-resembling protein-based vaccines thereby highlighting their application in tackling disorders, including HIV[67].

**Nanogels.** These gel-like polymer-based nanocarriers offer numerous advantages over conventional drug delivery systems, including easy preparation, diverse carrying capabilities, and lowest cargo efflux, with applicability in various grounds. Their potential exceeds conventional applications in areas of bioelectronics, biochemistry, tissue regeneration, biomaterials, and wound healing, thereby holding promising applications in fields of vaccines, nucleic acids, and immunotherapy[68].

### Multifactorial Bio-Impact of Nanoparticulate System from Cellular Disruption to its Therapeutic Potential

Nanoparticles (NPs) within the biological systems are complex and multifaceted, indicating potential impact on numerous processes occurring within cancerous cells, including disruption of cellular homeostasis, induction of nucleic acid denaturation, causing altered mitochondrial membrane potential, ultimately resulting in impaired lipid, protein, and mitochondrial activity [69]. The production of reactive oxygen species (ROS) and oxidative stress leads to apoptosis activation via cytochrome-c expression and resultantly intracellular cation deposition, that ultimately increases these deleterious effects. Furthermore, the effects of NPs-induced inflammation contribute to their variability in prompting numerous biological pathways [70]. In addition to the intracellular disruption, NPs also possess a propensity to interact with the sulfhydryl groups and inactivate essential enzymes of the metabolic transport chain within the mitochondrion, thus undermining the cell's integrity [71]. It also interacts negatively with their affinity to plasma proteins and the phosphorus DNA moieties, thereby interfering with the DNA replication processes and possibly leading to genotoxicity[72].

Interestingly,  $Zn^{2+}$  and  $Ca^{2+}$  ions have been noticed to be specifically displaced with silver nanoparticles (AgNPs), thereby interfering with the bio-interaction portfolio. Nevertheless, these intracellular outcomes are not the only effects of NPs but also exhibit potential applications in antimicrobial therapy based on their capacity to disrupt biofilm and microbial structures [73]. Furthermore, their ability to serve as drug carriers enabled them to deliver therapeutic medicaments to specific locations or tissues with a targeted delivery of the treatment components by taking advantage of enhanced permeability and retention (EPR) effect [74]. Moreover, their ability to induce endocytosis has enabled the formulation of viable and specific therapeutic measures.

### Challenges and Limitations of Personalized Medicine in Cancer Treatment

#### Complexity of Tumor Heterogeneity

Tumor heterogeneity is another hurdle in the introduction of personalized treatment. Tumors are not static entities; they develop genetically and physically throughout time, resulting in sub-clonal populations with unique genetic profiles[73]. This complexity affects treatment planning since tumors' genetic landscapes might alter throughout therapy, necessitating

frequent genomic analysis and adaptive treatment regimens. Personalized treatment must consequently be dynamic and responsive to tumor progression, resulting in a resource-intensive strategy[75].



**Figure 4 Challenges and limitations associated with the personalized medication system**

### The biological complexity of tumors

Cancer is a highly varied illness, both within and between tumors. This biological diversity creates substantial obstacles for tailored therapy. Inter-tumoral heterogeneity refers to genetic and epigenetic differences between tumors in different patients, whereas intra-tumoral heterogeneity refers to the presence of many cell types inside a single tumor [76]. Such diversity makes it difficult to identify universal biomarkers and predict therapy responses. Furthermore, tumor evolution during therapy, driven by selective forces, might result in clonal proliferation and acquired resistance [77]. To address this, dynamic monitoring mechanisms must be implemented, as well as medicines that target numerous pathways at the same time.

### Technological barriers

While genomic and proteomic technologies have improved tremendously, there are still limitations in clinical use. High-throughput sequencing and bioinformatics techniques necessitate extensive expertise and infrastructure, which are frequently unavailable in resource-constrained environments [78]. Furthermore, doctors and researchers have major hurdles when interpreting large amounts of genetic data and separating actionable changes from passenger mutations. Standardization of tests and reproducibility across platforms are also key concerns. Discrepancies in biomarker detection and interpretation might cause variability in treatment recommendations, weakening the validity of personalized medicine [79].

### Financial and Accessibility Issues

Patients have limited access to genetic testing, targeted medicines, and immunotherapies due to their high prices, particularly in low- and middle-income countries (LMICs). For example, CAR-T cell therapy can cost more than \$400,000 per patient, rendering it unsustainable for many healthcare systems [80, 81]. Patients face financial burden due to varying insurance coverage and reimbursement regulations for personalized medical therapies. Addressing these gaps necessitates global initiatives to cut prices, increase healthcare coverage, and subsidize critical technology in underserved areas[80].

### Limited data on long-term outcomes

While several personalized medicine treatments have shown promise in clinical trials, there is no evidence of their long-term safety, efficacy, or impact on survival. Real-world evidence is required to validate their efficacy across several demographics and cancer subtypes [4]. This necessitates rigorous post-marketing surveillance and longitudinal

investigations that track patient outcomes over time.

## Ethical and regulatory concerns

The application of personalized medicine presents ethical and regulatory concerns, particularly with genetic testing and data privacy. Patients may experience psychological discomfort or discrimination because of their genetic risk profiles, demanding strong counseling and protective laws [82]. Ethical considerations like genetic privacy, prejudice, and decision-making are crucial in personalized medicine. As genetic data becomes more important in cancer treatment, insurers, businesses, and educational institutions may engage in genetic discrimination. Furthermore, the transfer and storage of sensitive genetic information raise concerns regarding permission, patient autonomy, and data security. Ensuring ethical norms and strong legal frameworks is critical for protecting patient rights and privacy while encouraging responsible use of genetic information [83].

## Complications and Challenges Associated with nanoparticulate therapy

**Cytotoxicity: Exploring Their Cytotoxic Effects on Non-Cancerous Cells** Nanoparticles (NPs), with their dimensions often less than 100 nanometers, have emerged as a revolutionary tool in medicine and various other fields. However, their extremely small size raises concerns regarding their potential to interact with and disrupt intracellular biochemical processes. This interaction can occur with various biological structures, including the cell wall, organelles, and even nucleic acids, potentially impacting the normal functioning of healthy cells [84].

**In vivo Concerns and the Uncertain Fate of NPs:** One of the most pressing concerns is the unknown fate of various nanobiotechnological products, particularly nanoparticles (NPs) of different sizes and materials. After entering the body, these NPs can interact with various biological components and distribute them to different organs. However, the precise pathways and long-term impact of this distribution remain largely unknown, creating uncertainty regarding their long-term effects on biological systems[70].

**Dose-Dependent Cytotoxicity: A Threat to Non-Cancerous Cells:** Several studies have demonstrated the dose-dependent cytotoxic effects of NPs on non-cancerous cells. For instance, AgNPs biosynthesized using *Streptomyces* sp. NH28 biomass exhibited a significant reduction in cell viability ( $82.9 \pm 7.5\%$ ) in mammalian cells at concentrations as low as 25  $\mu\text{g/mL}$  (IC<sub>50</sub> 64.5  $\mu\text{g/mL}$ )[85]. Similarly, starch-stabilized AgNPs (20 nm) have been shown to decrease the viability of murine cells at concentrations of 10  $\mu\text{M}$ . These findings highlight the potential for unintended damage to healthy cells by NPs, even at relatively low concentrations. This raises concerns about the broader impact of such damage on organ function and overall health[86].

**The Need for Comprehensive Research** To address these concerns and ensure the safe and responsible development of nanotechnology; comprehensive research is crucial. This research should focus on the following:

- Understanding the in vivo fate and distribution of NPs: This includes investigating their interactions with biological components, potential accumulation in organs, and long-term effects on health.
- Developing safe and effective NP designs: This includes optimizing the size, shape, and surface properties of NPs to minimize toxicity and maximize desired therapeutic effects[87].

The cytotoxicity and biocompatibility Evaluation of NPs involves conducting rigorous studies to assess the potential harm of NPs on various cell types and tissues. Establishing regulatory frameworks: This includes developing guidelines and regulations for the development, testing, and use of nanomaterials to ensure safety and efficacy[88]. By addressing these concerns and conducting thorough research, we can unlock the vast potential of nanotechnology while minimizing potential risks and ensuring its responsible and beneficial development. The biological actions and behavior of NPs are significantly influenced by various factors, including the following:

## Functionalization

Different functionalization approaches can alter the cytotoxicity and antibacterial properties of NPs. For example, SeNPs functionalized with poly-L-lysine (PLL) exhibited high levels of cytotoxicity and genotoxicity in TR146 (SCC), HaCaT, and Caco-2 cells, while PAA- and PVP-coated SeNPs showed no toxicity toward *E. coli*, *S. aureus*, or *S. cerevisiae* BY4741[89].

**Materials used in fabrication:** The specific material used to fabricate the NPs can also impact their cytotoxicity. For instance, commercially available AgNPs (15 and 100 nm) have been shown to induce significant toxicity in murine hepatocytes compared to NPs of manganese oxide, molybdenum, aluminum, iron oxide, or tungsten [90].

**Functionalization: Tailoring the Nanoscale Armor** The remarkable potential of nanoparticles hinges heavily on their surface chemistry and the strategic placement of targeting ligands or antibodies. These functionalities, often referred to as bioconjugates, determine the fate of the nanoparticles and their interactions with biological systems. Tailoring the surface properties of nanoparticles presents significant challenges, as the stability of the cargo, protection from enzymatic degradation, and evasion of the reticuloendothelial system (RES) must be meticulously considered [91]. Polymeric and organic nanomaterials offer remarkable advantages in this regard, readily accepting surface modifications with antibodies, peptides, or other biomolecules. This attribute enables them to efficiently encapsulate and deliver therapeutic agents or

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photosensitizers, paving the way for targeted therapies and diagnostics. Inorganic nanomaterials, on the other hand, pose greater challenges due to their inherent properties (e.g., fixed size, solid structure). While some can be surface-modified chemically or biologically, their limited cargo capacity restricts their functionality. Encapsulation with polymers, such as PEG or chitosan, offers a promising solution for inorganic nanoparticles, enabling them to carry biomolecules or drugs on their surface. However, the number and types of biomolecules that can be attached to the surface remain limited, governed by potential interactions and competition among them [92]. In contrast, liposomes, with their core–shell structure, offer the unique ability to simultaneously encapsulate a multitude of therapeutic or imaging agents, expanding the therapeutic potential of such systems [93].

**Delivery and Targeting: Navigating the Biological Labyrinth** The intricate dance of delivery and targeting is influenced by a complex interplay of factors, including synthesis methods, functionalization strategies, local microenvironments, and administration routes. Nanoparticles can reach their designated destinations through two main pathways: passive and active targeting[94]. Passive targeting relies on the enhanced permeability and retention (EPR) effect, where nanoparticles exploit the leaky vasculature and impaired lymphatic drainage characteristic of tumor tissues. Conversely, active targeting leverages the power of specific ligands or antibodies that bind to unique receptors on target cells, enabling precise delivery and minimizing adverse effects on healthy tissues[95]. Despite the promising potential of active targeting, inherent challenges remain. Untargeted nanoparticles, lacking specific ligands or antibodies, are more susceptible to off-target diffusion, accumulating in healthy tissues and potentially inducing unwanted cytotoxicity. Moreover, premature release of the therapeutic cargo or its degradation by the RES can significantly hinder the efficacy of nanoparticle-based therapies. Polymeric nanomaterials, liposomes, and micelles, with their well-defined structures and encapsulation capabilities, offer an advantage in this regard, providing greater protection and controlled release of therapeutic agents [88]. Unfortunately, the intricate interplay between the tumor microenvironment (TME) and intracellular biochemistry adds another layer of complexity to the delivery process. Factors such as cell type, disease state, and intercellular interactions can significantly influence the behavior of nanoparticles, making it challenging to predict their precise delivery and therapeutic outcomes. Therefore, meticulous investigation and thorough characterization are essential to fully understand the delivery capacity and biochemical interactions of drug-loaded nanoparticles within diverse biological systems[96].

## Case Studies & Clinical Applications

### Success Stories

Patients with non-small cell lung cancer (NSCLC) who have EGFR mutations respond effectively to tyrosine kinase inhibitors (TKIs) such as gefitinib and osimertinib. These medicines target the precise genetic change, resulting in better progression-free survival and quality of life [97]. Melanoma with BRAF Mutations: In patients with BRAF V600E mutations, targeted therapy such as vemurafenib and dabrafenib has resulted in significant responses, including longer progression-free survival and lower recurrence rates [98]. These examples demonstrate how precision medicine enhances clinical outcomes by specifically targeting specific genomic defects in cancer cells.

### Ongoing Clinical trials

**NCI-MATCH Trial (National Cancer Institute's Molecular Analysis for Therapy Choice):** This trial looks into the use of tailored therapeutics based on the molecular profiles of advanced malignancies. Patients are paired with experimental treatments based on certain genetic variations[99].

**IMvigor130:** IMvigor130 is a clinical trial investigating the efficacy of immune checkpoint inhibitors (atezolizumab) in patients with advanced urothelial cancer. This trial highlights the importance of customized immunotherapy in bladder cancer management based on PD-L1 expression [100]. These studies are critical for improving customized treatment options and increasing the therapeutic arsenal for diverse malignancies.

**Table 3: Numerous Examples eliminating the role of Targeted Therapies/Immunotherapies in cancer treatment**

Therapy Type	Example Drug/Method	Target/Mechanism	Cancer Type(s)	
<b>Targeted Therapy</b>	Imatinib	Tyrosine Inhibitor (ABL protein)	Kinase (BCR-fusion)	Chronic Myeloid Leukemia (CML)

Therapy Type	Example Drug/Method	Target/Mechanism	Cancer Type(s)
<b>Immunotherapy</b>	Trastuzumab	Monoclonal antibody (HER2 receptor)	HER2-positive Breast Cancer
	Gefitinib/Erlotinib	EGFR Inhibitor	Non-Small Cell Lung Cancer (NSCLC) with EGFR mutations
	Vemurafenib	BRAF Inhibitor	Melanoma with BRAF V600E mutation
	Olaparib	PARP Inhibitor	BRCA-mutated Ovarian and Breast Cancers
	Pembrolizumab/Nivolumab	Immune Checkpoint Inhibitor (PD-1/PD-L1)	Melanoma, NSCLC, various other malignancies
	Tisagenlecleucel	CAR-T cell therapy	Acute Lymphoblastic Leukemia (ALL)
	Bevacizumab	Monoclonal antibody (VEGF)	Various cancers (anti-angiogenesis)

## Future perspectives

Personalized medicine in cancer treatment is evolving due to technical advancements, deeper biological understanding, and novel therapeutic techniques. Several exciting advancements are on the horizon:

### Integration of Multi-Omic Data

The combination of genomes, proteomics, metabolomics, and epigenomics is predicted to improve our understanding of cancer biology and therapeutic responses. Multi-omics integration will enable more comprehensive tumor profile characterization and highly precise interventions [101].

### AI and Machine Learning

AI and machine learning algorithms are playing an increasingly essential role in customized medicine. These tools can evaluate complex datasets, predict treatment outcomes, and uncover potential drug targets. AI-driven clinical decision support systems have the ability to enhance treatment plans and improve patient outcomes [102].

### Advances in liquid biopsy and real-time monitoring

The continuous development of liquid biopsy technologies will allow for non-invasive, real-time monitoring of disease progression and therapy efficacy. Advancements in ctDNA, circulating tumor cells (CTCs), and exosomal analysis will enhance early detection, resistance monitoring, and adaptive therapy strategies [28].

### Gene Editing and CRISPR-Based Therapy

CRISPR-Cas9 technology provides unprecedented opportunities for cancer treatment. By targeting and editing specific oncogenic mutations, CRISPR-based therapeutics have the ability to rectify genetic defects, overcome resistance, and augment immunotherapies [103].

### CRISPR Gene Editing

CRISPR/Cas9 technology shows promise for precisely editing cancer cells' genomes and correcting genetic mutations that cause carcinogenesis. This method has the potential to reduce the requirement for ongoing therapy by repairing underlying genetic defects [104].

### Nanoparticle-Based Therapies

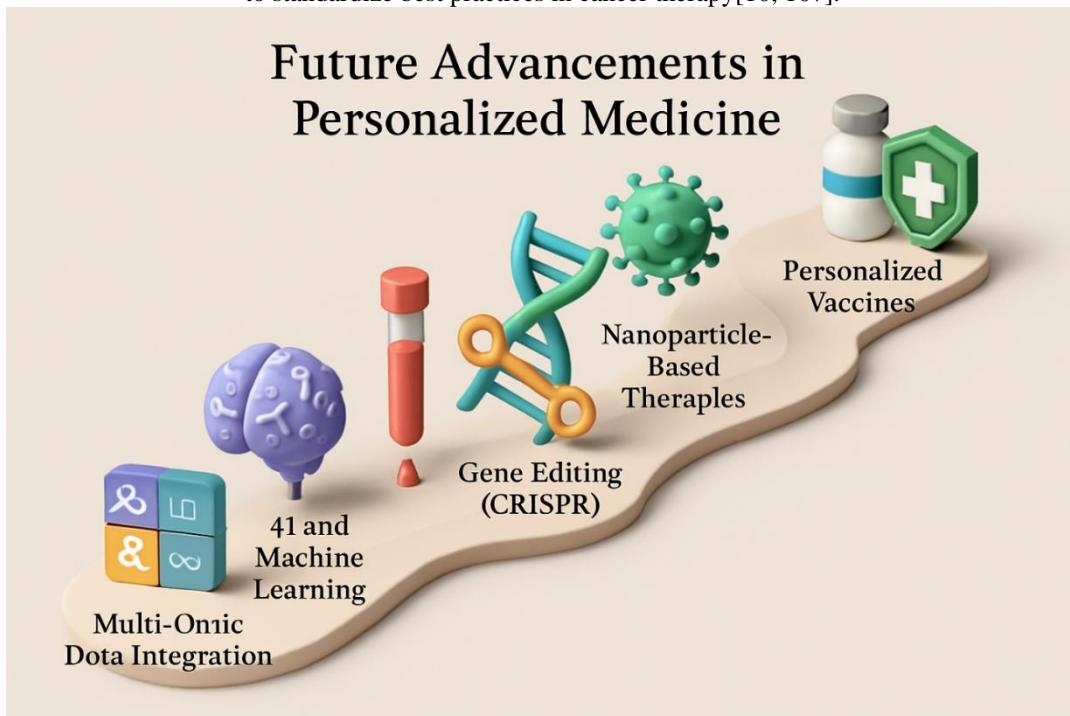
Nanotechnology is being used to develop drug delivery systems that can precisely target cancer cells. Nanoparticles improve therapeutic agent selectivity and absorption, reducing off-target effects while enhancing efficacy [105].

### Personalized Vaccines

Personalized cancer vaccines are emerging as a new approach to cancer immunotherapy. These vaccines are designed to target an individual's tumor profile, which includes mutations, antigens, and other unique molecular markers. By boosting the patient's immune system to target specific cancer cells, tailored vaccines could give long-lasting protection against cancer recurrence [106].

### Integrating Personalized Medicine in Standard Care

The incorporation of personalized medicine into ordinary oncology treatment is a big step toward more precise and individualized cancer care. By merging genetic testing, molecular profiling, and real-time data analysis into clinical decision-making, personalized medicine has the potential to improve treatment outcomes while reducing unnecessary harm. As data becomes more accessible and technology progresses, frequent use of tailored techniques has the potential to standardize best practices in cancer therapy [10, 107].



**Figure 5** Future perspectives of personalized/precision medication systems

## 2. CONCLUSION

Personalized medicine is a paradigm shift in cancer therapy, focusing on precision and patient-centered care. Therapeutic efficacy, adverse effects, and quality of life have all improved when medicines are tailored to patients' unique genetic and molecular profiles. However, achieving customized medicine's full promise requires overcoming considerable difficulties. These include tumor heterogeneity, technological limitations, budgetary limits, and ethical concerns. Addressing these problems and expanding the availability of customized cancer care will require collaborative research, technological innovation, and equitable policies. As science and technology advance, customized medicine will continue to reshape oncology, providing hope for more effective, sustainable, and egalitarian cancer therapies.

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