Review

Translational Nanotechnology in Oncology: Integrating Nanoscale Innovation into Precision Cancer Diagnosis and Therapy

Ashutosh Kumar Maurya [†], Sweta Saswati Rath [†], Ashish Kumar Maurya, V.B. Sameer Kumar [*], Jordi Muntane [*], Rajendra Pilankatta [*]

Posted Date: 4 November 2025

doi: 10.20944/preprints202510.2360.v2

Keywords: nanomedicine; targeted drug delivery; nanocarriers; theranostics; nanodiagnostics

 doi:10.20944/preprints202510.2360.v2

Review

Translational Nanotechnology in Oncology: Integrating Nanoscale Innovation into Precision Cancer Diagnosis and Therapy

Ashutosh Kumar Maurya [1,†], Sweta Saswati Rath [2,†], Ashish Kumar Maurya [3], V.B. Sameer Kumar [4*], Jordi Muntane [5,*] and Rajendra Pilankatta [1,*]

[1] Department of Biochemistry & Mol. Biology, Central University of Kerala, Kasaragod, Kerala, India, 671316
[2] Department of Zoology, Central University of Kerala, Kasaragod, Kerala, India, 671316
[3] Institute of Engineering & Technology, Bundelkhand University, Jhansi, Uttar Pradesh, India, 284128
[4] Department of Genomic Science, Central University of Kerala, Kasaragod, Kerala, India, 671316
[5] Instituto de Biomedicina de Sevilla, Universidad de Sevilla, Sevilla, Spain, 41004
* Correspondence: ashu644@gmail.com (V.B.S.K.); ashu@cukerala.ac.in (J.M.); praj74@gmail.com (R.P.)
† These authors contributed equally to this work.

Abstract

Cancer remains one of the most formidable challenges in global health, characterized by immense biological complexity, heterogeneity, and resistance to conventional therapies. Despite significant advances in molecular biology and immuno-oncology, limitations in early detection, targeted delivery, and therapeutic precision continue to hinder effective management. Over the past two decades, nanotechnology has emerged as a transformative platform, offering novel strategies for both cancer diagnostics and treatment. Engineered nanomaterials—ranging from liposomes and polymeric nanoparticles to quantum dots and metallic nanostructures—enable precise tumor targeting, enhanced imaging resolution, and controlled therapeutic release. In diagnostics, nanoscale biosensors and imaging probes have revolutionized the sensitivity and specificity of biomarker detection and visualization, while in therapeutics, nanocarriers have minimized systemic toxicity and improved pharmacokinetics. Recent innovations, including smart and stimuli-responsive nanoplatforms, nanorobotics, and integrated "theranostic" systems, are reshaping personalized cancer care. However, translational hurdles persist, particularly in large-scale manufacturing, biosafety, and regulatory validation. This review critically examines the evolution of nanotechnology in oncology, emphasizing current applications, clinical progress, and future prospects toward achieving precision nanomedicine in cancer diagnosis and therapy.

Keywords: nanomedicine; targeted drug delivery; nanocarriers; theranostics; nanodiagnostics

1. Introduction

Cancer continues to be a major global health challenge, representing one of the leading causes of death worldwide. According to the Global Cancer Observatory (GLOBOCAN), more than 19 million new cancer cases and nearly 10 million deaths were reported in 2022, with projections indicating a substantial rise in incidence over the coming decades due to aging populations and lifestyle transitions [1,2]. Despite considerable progress in diagnostic imaging, molecular profiling, and targeted therapies, survival outcomes remain suboptimal for many malignancies—particularly those diagnosed at advanced stages or characterized by aggressive biology [3,4].

1.1. Biological complexity and heterogeneity of tumors

Cancer is not a single disease but a multifaceted collection of disorders driven by diverse genetic, epigenetic, and microenvironmental alterations [5]. Intratumoral heterogeneity—manifested through

 doi:10.20944/preprints202510.2360.v2

variations in cellular composition, signaling pathways, and metabolic states—contributes to therapeutic resistance and disease relapse [6,7]. Furthermore, the dynamic interactions between tumor cells and the surrounding stroma, immune components, and extracellular matrix further complicate therapeutic efficacy [8]. Such complexity underscores the limitations of conventional "one-size-fits-all" approaches and necessitates precision oncology, where diagnosis and treatment are tailored to individual tumor profiles [9].

1.2. The need for precision and personalization

Precision medicine aims to integrate molecular biomarkers, genetic signatures, and patient-specific factors into clinical decision-making [10]. However, while genomic sequencing and targeted therapies have advanced this paradigm, several challenges persist—including limited accessibility, high cost, and the inability to capture real-time tumor evolution [11,12]. Effective precision oncology therefore requires dynamic, minimally invasive, and spatially resolved diagnostic tools capable of tracking disease progression and treatment response at the molecular level [13].

1.3. Nanotechnology as a transformative enabler

Nanotechnology, broadly defined as the manipulation and application of materials at the nanoscale (1–100 nm), offers unprecedented opportunities to bridge the gap between molecular insight and clinical intervention [14,15]. The nanoscale dimension allows for enhanced interaction with biological systems, enabling controlled delivery of therapeutics, sensitive detection of biomarkers, and improved imaging resolution [16]. Importantly, nanomaterials can be engineered for multifunctionality—simultaneously serving as diagnostic, therapeutic, and monitoring platforms ("theranostics") [17].

Over the past two decades, nanomedicine has evolved from a conceptual innovation to a rapidly expanding field with tangible clinical applications [18]. Liposomal formulations such as Doxil® (pegylated liposomal doxorubicin) and Abraxane® (albumin-bound paclitaxel) have demonstrated how nanocarriers can enhance drug solubility, alter pharmacokinetics, and reduce systemic toxicity compared to conventional chemotherapies [19,20]. Concurrently, advances in nanodiagnostics, including nanoparticle-based biosensors and imaging probes, have markedly improved sensitivity for early cancer detection [21].

1.4. Scope of this review

This review provides a comprehensive overview of how nanotechnology is redefining the landscape of cancer management. We first summarize the limitations of current diagnostic and therapeutic modalities, followed by an exploration of the design principles and biological mechanisms underlying nanomaterial-based systems. We then discuss recent advances in nanotechnology-driven diagnostics and therapies, highlight examples of clinical translation and ongoing trials, and examine the challenges that continue to impede widespread implementation. Finally, we explore emerging trends—such as smart nanoplatforms, artificial intelligence (AI) integration, and personalized nanomedicine—that are shaping the next generation of cancer care.

2. Conventional Cancer Modalities: A Brief Overview

Cancer diagnosis and treatment have traditionally relied on well-established clinical modalities. Despite decades of progress, conventional approaches exhibit limitations that underscore the need for more precise and targeted strategies [22].

2.1. Diagnostic Methods

Histopathology remains the gold standard for cancer diagnosis, offering detailed morphological and cellular insights through tissue biopsies. Despite its high specificity, it is inherently invasive and may fail to represent the full extent of tumor heterogeneity [23]. Non-invasive imaging modalities

 doi:10.20944/preprints202510.2360.v2

such as magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET) provide valuable anatomical and functional information on tumors. MRI offers superior soft-tissue contrast, CT delivers precise anatomical detail, and PET enables metabolic imaging through radiolabeled tracers [24]. However, these modalities often lack adequate sensitivity for early-stage tumor detection and do not capture molecular-level alterations [25]. Molecular diagnostic assays—including polymerase chain reaction (PCR), immunohistochemistry (IHC), and next-generation sequencing (NGS)—enable the detection of genetic mutations, epigenetic changes, and protein biomarkers. Although these approaches enhance diagnostic precision and support personalized therapy decisions, they are typically costly, time-intensive, and require high-quality biological samples [26].

2.2. Therapeutic Modalities

Surgical resection remains the primary curative approach for localized tumors; however, achieving complete removal can be difficult due to factors such as tumor location, local invasion, or the presence of micrometastases [27]. Radiotherapy employs ionizing radiation to eradicate malignant cells or inhibit their proliferation, yet despite technological advances such as intensity-modulated radiotherapy (IMRT), collateral damage to adjacent healthy tissues remains a significant concern [28]. Chemotherapy, which utilizes cytotoxic agents to disrupt cell division, is often limited by severe off-target toxicity, the emergence of drug resistance, and suboptimal tumor selectivity [29]. Immunotherapy—encompassing checkpoint inhibitors and chimeric antigen receptor (CAR)-T cell therapies—has transformed the therapeutic landscape by harnessing the immune system's power to combat cancer; nevertheless, clinical responses vary considerably among tumor types, and immune-related adverse events can be severe or even life-threatening [30]. Similarly, targeted therapies using small molecules or monoclonal antibodies against specific oncogenic pathways have shown success in genetically defined patient subsets, but resistance commonly arises through pathway redundancy and compensatory signaling mechanisms [31].

2.3. Limitations of Conventional Modalities

Despite considerable progress in oncology, conventional diagnostic and therapeutic modalities continue to face major limitations [32]. Chemotherapy and radiotherapy often lack specificity, leading to collateral damage in healthy tissues, systemic toxicity, and restricted dosing potential [32]. Tumor heterogeneity and adaptive resistance mechanisms further contribute to therapeutic failure and disease relapse [33]. Additionally, poor solubility, rapid systemic clearance, and limited accumulation of drugs within tumor tissue significantly impair treatment efficacy [34]. On the diagnostic front, existing methods frequently fail to detect malignancies at early and potentially curable stages, particularly in heterogeneous or micro-metastatic tumors [35]. These persistent challenges underscore the urgent need for innovative strategies that enhance tumor selectivity, minimize systemic toxicity, and enable real-time monitoring of therapeutic response—a domain where nanotechnology-based approaches demonstrate exceptional potential [36].

3. The Emergence of Nanotechnology in Oncology

Nanotechnology—the engineering and manipulation of materials at the nanoscale (1–100 nm)—has rapidly transformed biomedical research. In oncology, **nanomedicine** leverages the unique physical, chemical, and biological properties of nanomaterials to improve cancer detection, delivery, and therapy [37]. Nanoparticles can interact with biomolecules at the cellular and molecular level, offering solutions to limitations of conventional modalities, such as poor solubility, low specificity, and systemic toxicity [38].

 doi:10.20944/preprints202510.2360.v2

3.1. Definition and Principles of Nanotechnology in Medicine

Nanomedicine integrates diagnostic, therapeutic, and theranostic applications of nanoscale materials, capitalizing on their unique physicochemical properties to advance cancer management [39]. A key feature of nanoparticles lies in their size-dependent characteristics—marked by a high surface-area-to-volume ratio, enhanced chemical reactivity, and tunable optical, magnetic, or electronic behavior [39]. Through strategic surface functionalization with ligands, antibodies, or polymers, nanomaterials can be engineered for active targeting of tumor-specific receptors and biomolecular pathways [40]. In addition, advanced nanocarriers enable controlled and stimuli-responsive drug release triggered by tumor-associated cues such as pH, temperature, or enzymatic activity, thereby optimizing the therapeutic index and minimizing systemic toxicity [41]. Collectively, these attributes facilitate superior tumor accumulation, improved biodistribution, and seamless integration of diagnostic and therapeutic functions, establishing nanomedicine as a cornerstone of precision oncology [42].

3.2. Types of Nanomaterials in Cancer

A wide variety of nanomaterials have been developed and optimized for oncological applications, each offering distinct structural and functional advantages [43]. Liposomes, spherical vesicles capable of encapsulating both hydrophilic and hydrophobic drugs, are among the most clinically advanced systems, exemplified by the FDA-approved formulation Doxil® [43]. Polymeric nanoparticles, composed of biodegradable materials such as PLGA and PEG, enable controlled drug release, enhanced stability, and surface modification for targeted delivery [44]. Dendrimers, with their highly branched architecture and abundant surface functional groups, provide versatile platforms for loading drugs, genes, or imaging agents [45]. Quantum dots (QDs), semiconductor nanocrystals with size-dependent fluorescence, are particularly valuable in cancer imaging and diagnostics [46]. Metallic nanoparticles—including gold, silver, and iron oxide nanostructures—offer multifunctionality, serving as agents for photothermal therapy, imaging enhancement, and drug delivery [47]. Moreover, exosomes and biomimetic nanoparticles, derived from natural cellular vesicles, present promising biocompatible carriers for targeted drug delivery and intercellular communication [48]. The choice of nanomaterial depends on the intended application—diagnostic, therapeutic, or theranostic—allowing tailored designs that integrate precision, efficacy, and safety [49].

3.3. Mechanisms of Tumor Targeting

Nanoparticles exploit both passive and active targeting mechanisms to enhance tumor specificity and therapeutic precision [50]. Through the enhanced permeability and retention (EPR) effect, nanoparticles preferentially accumulate in tumor tissues due to the leaky vasculature and impaired lymphatic drainage characteristic of the tumor microenvironment [50]. In addition, active targeting strategies employ surface-functionalized ligands such as antibodies, peptides, or aptamers that selectively bind to overexpressed receptors on cancer cells, thereby promoting cellular uptake and intracellular delivery [51]. Stimuli-responsive nanoparticle systems further improve specificity by releasing their therapeutic cargo in response to tumor-associated cues such as pH, redox potential, enzymatic activity, or temperature variations [52]. The combination of these targeting approaches enables nanomedicine to overcome major delivery barriers posed by the dense extracellular matrix, heterogeneous vasculature, and immune clearance mechanisms, ultimately improving therapeutic efficacy and safety [53].

3.4. Outlook

The emergence of nanotechnology has established a platform for precision oncology, bridging gaps in conventional cancer management. By integrating diagnostic and therapeutic functions, nanomedicine holds the potential to improve efficacy, reduce toxicity, and enable personalized

 doi:10.20944/preprints202510.2360.v2

cancer care [54]. Ongoing research continues to refine material design, targeting strategies, and multifunctional capabilities, paving the way for next-generation clinical translation[55].

4. Nanotechnology in Cancer Diagnostics

Accurate and early cancer detection is critical for improving patient outcomes. Conventional diagnostics often lack sensitivity, specificity, or the ability to capture tumor heterogeneity [56]. Nanotechnology addresses these challenges by providing molecular-level detection, high-throughput multiplexing, and real-time monitoring, enabling non-invasive and personalized diagnostic approaches [57,58].

4.1. Nanobiosensors for Early Detection

Nanobiosensors integrate nanomaterials with biological recognition elements such as antibodies, aptamers, nucleic acids, and enzymes to enable ultra-sensitive detection of cancer biomarkers, including DNA mutations, microRNAs (miRNAs), and proteins [59]. Metallic nanoparticles—particularly those composed of gold, silver, or platinum—amplify optical and electrochemical signals, achieving detection sensitivity down to the single-molecule level [60]. Similarly, carbon-based nanostructures like graphene and carbon nanotubes provide exceptional conductivity and large surface areas, facilitating label-free sensing approaches [61]. For instance, graphene oxide–based biosensors have successfully detected miR-21 at femtomolar concentrations in breast and colorectal cancers [62], while gold nanoparticle-based colorimetric assays enable visual identification of tumor markers through localized surface plasmon resonance (LSPR) shifts [63]. Furthermore, advances in multiplexed nanobiosensing allow simultaneous detection of multiple biomarkers, offering deeper insights into tumor heterogeneity and disease progression [64].

4.2. Nanoparticle-Enhanced Imaging

Nanoparticles have significantly enhanced the sensitivity and specificity of cancer imaging modalities, facilitating improved tumor visualization and functional assessment [65]. Superparamagnetic iron oxide nanoparticles (SPIONs) act as potent magnetic resonance imaging (MRI) contrast agents, improving soft tissue differentiation and lesion detection [66]. Gold nanoparticles (AuNPs), owing to their high X-ray attenuation, enhance computed tomography (CT) imaging contrast and enable precise delineation of tumor margins [67]. Similarly, quantum dots (QDs) offer tunable fluorescence properties suitable for long-term and multiplexed imaging of cancer biomarkers [68]. Beyond diagnostics, theranostic nanoparticles integrate imaging and therapeutic capabilities, allowing real-time monitoring of drug delivery, biodistribution, and treatment efficacy—an essential step toward image-guided precision oncology [69,70].

4.3. Nanotechnology in Liquid Biopsy

Liquid biopsy has emerged as a minimally invasive approach for detecting tumor-derived biomarkers, including circulating tumor cells (CTCs), extracellular vesicles (EVs), and circulating free DNA (cfDNA) [71]. Magnetic nanoparticles functionalized with specific antibodies such as EpCAM enable efficient capture and enrichment of CTCs from peripheral blood samples [72]. Plasmonic nanosensors can sensitively detect cfDNA and exosomes by monitoring localized refractive index changes associated with molecular binding events [73]. Additionally, advanced nanopore and nanowire-based sensors facilitate label-free detection of single nucleic acid molecules with sub-picomolar sensitivity, offering unprecedented analytical precision [74]. Collectively, these nanotechnology-enabled liquid biopsy platforms support early cancer diagnosis, real-time monitoring of therapeutic responses, and dynamic tracking of tumor evolution [75].

 doi:10.20944/preprints202510.2360.v2

4.4. Integration with Artificial Intelligence

The high-dimensional data generated by nanodiagnostics require advanced computational analysis. Artificial intelligence (AI) and machine learning (ML) algorithms identify subtle biomarker patterns, predict disease progression, and guide clinical decisions [76].

Integration of AI with nanoparticle-enhanced imaging has improved differentiation between malignant and benign lesions compared to conventional analysis [77]. This convergence supports intelligent, predictive, and personalized diagnostics[78,79].

4.5. Outlook

Nanotechnology-based diagnostics represent a paradigm shift toward precision oncology, providing sensitive, specific, and real-time monitoring. Integration with liquid biopsy, imaging, and AI is expected to accelerate clinical translation, enabling dynamic, patient-specific cancer management [80].

5. Nanotechnology in Cancer Therapy

Conventional cancer therapies often suffer from poor tumor selectivity, systemic toxicity, and resistance. Nanotechnology offers innovative solutions by enhancing drug delivery, gene therapy, immunomodulation, and combination therapies, while minimizing off-target effects [81,82].

5.1. Nanoparticle-Based Drug Delivery Systems

Nanocarriers substantially enhance the pharmacokinetics, bioavailability, and tumor selectivity of chemotherapeutic agents [83]. Liposomal formulations, such as Doxil®, encapsulate cytotoxic drugs within lipid bilayers, reducing systemic toxicity while improving tumor accumulation through enhanced permeability and retention (EPR) [84]. Polymeric nanoparticles enable controlled and sustained drug release, customizable surface chemistry, and co-delivery of multiple agents to achieve synergistic therapeutic effects [85]. Dendrimers, owing to their highly branched and uniform structures, allow precise drug loading and functionalization with targeting ligands or imaging moieties [86]. Collectively, these nanocarriers leverage both passive targeting via the EPR effect and active targeting through ligand-mediated interactions, achieving improved tumor specificity and therapeutic efficacy [87].

5.2. Photothermal and Photodynamic Therapy

Photothermal therapy (PTT) and photodynamic therapy (PDT) leverage light-activated nanomaterials to induce selective tumor ablation. Gold nanorods are widely used in PTT for their ability to convert near-infrared light into localized heat, enabling precise tumor destruction with minimal invasiveness [88]. Graphene-based nanoplatforms further enhance therapeutic efficacy through superior photothermal conversion efficiency and high drug-loading capacity [89]. In PDT, photosensitizer-loaded nanoparticles generate cytotoxic reactive oxygen species (ROS) upon light irradiation, triggering apoptosis and oxidative stress within tumor tissues [90]. These light-responsive nanostrategies provide spatiotemporal control over therapeutic activation, thereby minimizing collateral damage to healthy tissues and improving safety profiles [91].

5.3. Gene and RNA Delivery

Nanoparticles have emerged as versatile carriers for nucleic acid–based therapeutics, including siRNA, mRNA, and CRISPR components, enabling precise gene silencing or protein expression within tumor cells. Lipid-based nanoparticles are particularly effective for mRNA delivery, as they protect fragile nucleic acids from enzymatic degradation while ensuring efficient cellular uptake and cytoplasmic release [92]. Polymeric and dendrimer-based nanocarriers further enhance siRNA transfection efficiency and provide tunable surface properties that minimize immunogenicity and

 doi:10.20944/preprints202510.2360.v2

off-target effects [93]. By enabling targeted modulation of oncogenes, drug-resistance pathways, and immune-regulatory genes, these nanocarrier systems expand the therapeutic landscape of oncology beyond conventional small molecules and biologics [94].

5.4. Immunomodulation and Cancer Vaccines

Nanocarrier-based systems play a pivotal role in augmenting cancer immunotherapy by enhancing antigen presentation and immune activation, thereby improving therapeutic efficacy [95]. Nanoparticle-based vaccines are designed to co-deliver tumor-associated antigens together with immune adjuvants, effectively stimulating antigen-presenting cells and eliciting robust cytotoxic T-cell responses [96]. In addition, nanocarrier conjugation with immune checkpoint inhibitors enables targeted delivery to tumor sites, reducing systemic exposure and mitigating immune-related adverse effects [97]. These nanotechnology-driven strategies can be integrated synergistically with other therapeutic modalities, such as chemotherapy or phototherapy, to overcome tumor-induced immune evasion and achieve more durable antitumor immunity [98].

5.5. Combination Nanotherapies

Nanotechnology has opened new avenues for multimodal cancer treatment strategies that combine chemotherapy, phototherapy, radiotherapy, and immunotherapy to achieve synergistic therapeutic outcomes. In chemo-photothermal therapy, nanoparticles are engineered to co-deliver chemotherapeutic drugs alongside photothermal agents, thereby enhancing tumor ablation through simultaneous chemical cytotoxicity and localized hyperthermia [99]. Radio-nanotherapy employs radioisotope-loaded nanoparticles to achieve targeted radiotherapeutic effects while minimizing off-target radiation exposure and collateral tissue damage [100]. Immuno-nanotechnology approaches further integrate nanocarriers with immune-modulating agents to enhance antigen presentation and cytotoxic drug delivery, promoting robust antitumor immune responses [101]. Collectively, these combination strategies harness complementary mechanisms of action, overcoming the inherent limitations of single-modality treatments and paving the way for more effective, multimodal cancer therapy paradigms [102].

5.6. Outlook

Nanotechnology-based cancer therapies offer precision, selectivity, and multifunctionality, addressing the shortcomings of conventional treatment. Future development will focus on stimuli-responsive platforms, combination strategies, and integration with diagnostics, paving the way for personalized and highly effective nanomedicine [103,104].

6. Clinical Translation and Current Trials

Despite impressive preclinical results, translating nanotechnology-based cancer therapies into clinical practice remains challenging. A growing number of FDA-approved nanomedicines and ongoing clinical trials, however, underscore the promise of nanotechnology in oncology [105].

6.1. FDA-Approved Nanomedicines

Several nanotechnology-based therapeutics have already gained regulatory approval, marking significant milestones in the clinical translation of nanomedicine. Doxil®, a liposomal formulation of doxorubicin, reduces cardiotoxicity while enhancing tumor accumulation and therapeutic efficacy [106]. Abraxane®, composed of albumin-bound paclitaxel nanoparticles, improves solubility and facilitates efficient drug delivery to tumors [107]. Similarly, Onivyde®, a liposomal formulation of irinotecan, exhibits superior pharmacokinetic properties and clinical benefits in the management of metastatic pancreatic cancer [108]. Collectively, these approved nanomedicines exemplify the feasibility of nanoparticle-based therapeutics in oncology, offering improved efficacy, reduced

 doi:10.20944/preprints202510.2360.v2

systemic toxicity, and more favorable pharmacokinetic and biodistribution profiles compared to conventional drug formulations [109].

6.2. Ongoing Clinical Trials

Multiple nanotechnology-based therapeutic approaches are currently under clinical investigation across diverse malignancies. Liposomal formulations of chemotherapeutic agents have demonstrated efficacy in breast, ovarian, and lung cancers, providing enhanced tumor accumulation and reduced systemic toxicity [110]. Polymeric nanoparticles are being evaluated for the targeted delivery of siRNA and mRNA in both solid tumors and hematologic malignancies, aiming to overcome biological barriers and improve gene-silencing efficiency [111]. Additionally, gold nanoparticles and photothermal nanomaterials are being explored in combination with imaging-guided therapies to enable simultaneous diagnosis and treatment [112]. Collectively, these ongoing clinical trials seek to validate promising preclinical outcomes while optimizing dosing regimens, tumor-targeting efficiency, and safety profiles for successful clinical translation [113].

6.3. Translational Barriers

Despite the remarkable potential of nanomedicine, several barriers continue to hinder its broad clinical translation. Large-scale manufacturing remains a major challenge, as ensuring reproducibility in nanoparticle size, surface characteristics, and drug-loading efficiency is technically demanding [114]. In addition, regulatory hurdles persist due to the lack of standardized global guidelines for nanoparticle characterization, pharmacokinetic profiling, and toxicological evaluation, which collectively delay clinical approval [115]. Furthermore, the complex fabrication processes and stringent quality control requirements substantially elevate production costs, posing obstacles to commercialization and large-scale clinical accessibility [116].

6.4. Safety and Biocompatibility Considerations

Nanomaterials must demonstrate favorable biocompatibility, minimal immunogenicity, and predictable biodistribution [117]. However, several safety concerns remain critical for their clinical translation. Rapid recognition by the mononuclear phagocyte system often leads to immune clearance, thereby reducing nanoparticle circulation time and tumor accumulation [118]. In addition, certain metallic or non-biodegradable nanoparticles may persist and accumulate in organs such as the liver, spleen, or kidneys, resulting in off-target and organ-specific toxicities [119]. Long-term safety considerations, including chronic exposure effects and incomplete biodegradation, also require systematic investigation [120]. Therefore, comprehensive preclinical modeling, detailed pharmacokinetic assessments, and rigorous clinical monitoring are essential to ensure patient safety and optimize the therapeutic index of nanomedicine-based interventions [121].

6.5. Outlook

While clinical translation remains complex, FDA-approved nanomedicines and ongoing trials demonstrate tangible progress. Continued optimization of nanoparticle design, reproducibility, targeting, and safety assessment will accelerate the integration of nanotechnology into routine oncology care [122].

7. Challenges and Limitations

Despite significant advances, nanotechnology in oncology faces multiple challenges that impede widespread clinical adoption. These challenges span biological, technical, regulatory, and ethical domains [123].

7.1. Biological Barriers

 doi:10.20944/preprints202510.2360.v2

The tumor microenvironment (TME) imposes significant barriers to effective nanoparticle delivery and therapeutic efficacy. The dense extracellular matrix (ECM) acts as a physical obstacle that restricts nanoparticle penetration and uniform dispersion within solid tumors [124]. Moreover, the heterogeneous and often abnormal tumor vasculature results in irregular blood flow and variable vessel permeability, leading to uneven nanoparticle distribution across tumor regions [125]. Immune recognition and phagocytosis by macrophages further contribute to rapid clearance of nanoparticles from circulation, thereby diminishing their effective tumor accumulation [126]. In addition to these microenvironmental challenges, both inter- and intra-patient tumor heterogeneity complicate the design of universal targeting strategies, ultimately resulting in variable therapeutic responses and inconsistent clinical outcomes [127].

7.2. Nanotoxicology and Biodistribution

Safety considerations remain paramount for the successful clinical translation of nanomedicine. Accumulation of metallic or non-biodegradable nanoparticles in non-target organs such as the liver, spleen, and kidneys can lead to organ-specific toxicity and impaired function [128]. Additionally, certain nanomaterials may elicit immune or inflammatory responses through cytokine release or complement activation, potentially compromising systemic safety [129]. The long-term fate, biodegradation behavior, and clearance mechanisms of many nanoparticle formulations also remain incompletely understood, posing further uncertainties regarding chronic exposure risks [130]. Therefore, rigorous preclinical toxicological evaluation, comprehensive pharmacokinetic analysis, and long-term clinical monitoring are essential to ensure patient safety and establish regulatory confidence in nanomedicine-based therapeutics [131].

7.3. Reproducibility and Scalability

Manufacturing consistency remains a critical challenge in the large-scale development of nanomedicines. Achieving uniformity in nanoparticle size, surface chemistry, and drug-loading efficiency is technically demanding and often difficult to maintain across production batches [132]. Even minor variations in physicochemical characteristics can lead to significant differences in pharmacokinetics, biodistribution, and therapeutic efficacy, highlighting the issue of batch-to-batch variability [133]. Furthermore, translating laboratory-scale synthesis protocols to industrial-scale production without compromising quality, reproducibility, or functional performance remains a major technological and regulatory barrier [134].

7.4. Regulatory Challenges

Regulatory standardization continues to be a major obstacle in the clinical advancement of nanomedicine. Although regulatory frameworks are gradually evolving, the absence of comprehensive and harmonized guidelines across global agencies still limits the efficient approval of nanotherapeutics [135]. The complex physicochemical nature of nanoparticles necessitates extensive characterization, requiring detailed evaluation of parameters such as size, surface charge, stability, pharmacokinetics, and in vivo behavior to meet regulatory expectations [136]. Moreover, the inherent heterogeneity of nanomaterials—encompassing diverse compositions, architectures, and mechanisms of action—further complicates the establishment of universal approval pathways, delaying clinical translation and commercialization [137].

7.5. Ethical and Economic Considerations

Beyond scientific and regulatory barriers, socioeconomic and ethical considerations also influence the clinical translation of nanomedicine. The high cost of nanoparticle development and manufacturing, driven by complex design processes and stringent quality control, significantly elevates research and production expenses, potentially limiting patient accessibility and widespread adoption [138]. Moreover, the personalized nature of many nanomedicine-based therapies may

 doi:10.20944/preprints202510.2360.v2

disproportionately benefit patients in high-resource settings, thereby exacerbating existing disparities in global cancer care [139]. Ethical challenges related to informed consent and long-term safety also warrant careful attention, as patients must be adequately informed about potential unknown or delayed effects associated with nanomaterial exposure [140].

7.6. Outlook

While nanotechnology holds transformative potential, overcoming biological barriers, toxicity concerns, reproducibility issues, regulatory hurdles, and ethical challenges is essential for safe and equitable clinical translation. Ongoing interdisciplinary efforts in materials science, pharmacology, and regulatory science aim to address these limitations [141].

8. Emerging Trends and Future Perspectives

Nanotechnology is rapidly evolving, with next-generation platforms poised to redefine cancer diagnosis and therapy. Innovations focus on smart functionalities, integration with AI, preclinical modeling, and precision delivery systems[142].

8.1. Smart Nanoplatforms

Stimuli-responsive and multifunctional nanoparticles represent a major advancement in precision nanomedicine, offering adaptive responses to specific tumor microenvironmental cues. pH- and redox-responsive systems are designed to release therapeutic agents selectively within acidic or oxidative tumor niches, thereby enhancing drug localization and minimizing systemic toxicity [143]. Multi-modal nanoplatforms that integrate imaging, therapeutic, and monitoring functionalities within a single construct enable real-time theranostic applications, bridging diagnosis and treatment for personalized cancer management [144]. Furthermore, programmable nanoparticles capable of dynamically adapting to fluctuations in the tumor microenvironment allow for controlled drug release and improved therapeutic efficacy [145]. Collectively, these smart nanotechnologies aim to maximize the therapeutic index while minimizing off-target effects, paving the way for more precise and effective cancer interventions [146].

8.2. Integration with AI and Bioinformatics

Artificial intelligence (AI) and machine learning (ML) are transforming the landscape of personalized nanomedicine by enabling the analysis of complex, multidimensional datasets encompassing nanoparticle behavior, imaging outputs, and patient-specific genomic profiles. Predictive modeling tools assist in optimizing nanoparticle design and forecasting therapeutic responses, thereby enhancing formulation efficiency and precision [147]. The development of digital tumor twins—computational models that replicate patient tumor microenvironments—allows simulation of nanocarrier interactions, facilitating dosage optimization and improved delivery outcomes [148]. Furthermore, automated analysis of imaging and liquid biopsy data enhances early cancer detection, real-time treatment monitoring, and response prediction [149]. The integration of AI-driven analytics thus accelerates the translation of nanomedicine from bench to bedside by informing rational design strategies and enabling patient-specific therapeutic interventions [150].

8.3. Organoid and Microfluidic Tumor Models

Advanced preclinical models have emerged as powerful and physiologically relevant platforms for evaluating the efficacy and safety of nanomedicines. Patient-derived organoids closely mimic the three-dimensional architecture, genetic heterogeneity, and drug response patterns of native tumors, thereby providing a personalized and predictive testing environment [151]. Similarly, microfluidic tumor-on-chip systems replicate key features of the tumor microenvironment, including vascular flow, extracellular matrix composition, and immune cell interactions, allowing precise control and observation of nanoparticle dynamics [152]. These innovative models enable high-throughput

 doi:10.20944/preprints202510.2360.v2

screening, real-time monitoring, and mechanistic investigations, significantly reducing reliance on conventional animal models while improving translational relevance and predictive accuracy [153].

8.4. Nanorobotics and Precision Delivery Systems

Emerging nanorobotic systems represent a transformative frontier in precision oncology, offering unprecedented control over navigation, targeting, and therapeutic delivery at the microscale. These nanoscale devices are capable of actively traversing the bloodstream, penetrating tumor tissues, and releasing therapeutic payloads in a spatially and temporally controlled manner [154]. Magnetically guided or self-propelled nanorobots enhance tissue penetration and help overcome biological barriers that typically limit passive nanoparticle delivery, thereby improving intratumoral distribution and treatment efficacy [155]. Furthermore, programmable nanorobotic delivery vehicles can be engineered to sequentially release multiple therapeutic agents in response to specific tumor microenvironmental cues, enabling highly targeted and minimally invasive treatment strategies [156].

8.5. Outlook for Next-Generation Clinical Translation

The convergence of smart nanoplatforms, AI-guided design, advanced preclinical models, and nanorobotics sets the stage for personalized, multifunctional cancer therapies. Future efforts will focus on scalable manufacturing, regulatory harmonization, and safety validation to bring these technologies from the laboratory to widespread clinical use [157,158].

9. Concluding Remarks

Nanotechnology has profoundly reshaped the landscape of oncology, offering innovative solutions for both cancer diagnosis and therapy. By bridging molecular precision with clinical applicability, nanomedicine addresses key limitations of conventional modalities, including poor tumor selectivity, systemic toxicity, and therapeutic resistance.

9.1. Progress Made

In diagnostics, nanobiosensors, nanoparticle-enhanced imaging, and liquid biopsy technologies have enabled earlier, more accurate, and minimally invasive cancer detection. Therapeutically, liposomal, polymeric, and multifunctional nanoparticles have enhanced drug solubility, bioavailability, and tumor-targeting efficiency while minimizing off-target effects. The successful clinical translation of nanomedicines such as Doxil® and Abraxane® validates the feasibility and safety of nanoscale interventions. Emerging innovations — including smart nanoplatforms, artificial intelligence–driven design, organoid-based testing, and nanorobotics — herald the advent of next-generation precision oncology.

9.2. Remaining Gaps

Despite these achievements, several critical challenges persist. Biological barriers, such as tumor heterogeneity and immune-mediated clearance, continue to limit nanoparticle penetration and uniform intratumoral distribution. Safety and nanotoxicology concerns, particularly those related to long-term biodistribution, metabolism, and clearance, require comprehensive investigation. Additionally, challenges in manufacturing scalability, regulatory harmonization, and cost-effectiveness hinder the broad clinical adoption of nanotherapeutics. Overcoming these obstacles will necessitate sustained, interdisciplinary collaboration among materials scientists, oncologists, pharmacologists, engineers, and regulatory agencies.

 doi:10.20944/preprints202510.2360.v2

9.3. Vision for the Next Decade

The future of nanotechnology-driven oncology lies in developing personalized, multifunctional, and adaptive therapeutic systems. Patient-specific nanomedicines, guided by artificial intelligence and multi-omics profiling, will enable precision treatments with real-time monitoring and adaptive feedback. Integrated theranostic platforms are poised to unify diagnosis, therapy, and longitudinal monitoring into a single, seamless continuum of care. Furthermore, advances in nanorobotics and bioinspired delivery systems will drive the emergence of minimally invasive, targeted, and highly efficient cancer management strategies.

If realized, these innovations will transform cancer care from a reactive discipline into a predictive, preventive, and precision-driven paradigm, moving closer to the ultimate goal — the personalized and effective eradication of cancer.

Authors Contribution: Conceptualization: VBSK, RP, JM**;** Original manuscript drafting: AKM, SSR**;** Proofread and Edit: AKM

Acknowledgment: ICMR, Govt. of India**;** KSCSTE, Govt. of Kerala, India

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2023;73(3):209-49.
2. Wild CP, Weiderpass E, Stewart BW, editors. World Cancer Report 2020: Cancer Research for Cancer Prevention. Lyon: IARC; 2020.
3. Miller KD, Nogueira L, Devasia T, Mariotto AB, Yabroff KR, Jemal A, et al. Cancer treatment and survivorship statistics 2022. CA Cancer J Clin. 2022;72(5):409-36.
4. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics 2023. CA Cancer J Clin. 2023;73(1):17-48.
5. Hanahan D. Hallmarks of cancer: New dimensions. Cancer Discov. 2022;12(1):31-46.
6. McGranahan N, Swanton C. Clonal heterogeneity and tumor evolution: Past, present, and the future. Cell. 2017;168(4):613-28.
7. Dagogo-Jack I, Shaw AT. Tumour heterogeneity and resistance to cancer therapies. Nat Rev Clin Oncol. 2018;15(2):81-94.
8. Quail DF, Joyce JA. Microenvironmental regulation of tumor progression and metastasis. Nat Med. 2013;19(11):1423-37.
9. Garraway LA, Verweij J, Ballman KV. Precision oncology: An overview. J Clin Oncol. 2013;31(15):1803-5.
10. Collins FS, Varmus H. A new initiative on precision medicine. N Engl J Med. 2015;372(9):793-5.
11. Van Norman GA. Limitations of precision medicine. JACC Basic Transl Sci. 2016;1(5):494-503.
12. Dienstmann R, Vermeulen L, Guinney J, Kopetz S, Tejpar S, Tabernero J. Consensus molecular subtypes and the evolution of precision medicine in colorectal cancer. Nat Rev Cancer. 2017;17(2):79-92.
13. Wan JC M, Massie C, Garcia-Corbacho J, Mouliere F, Brenton JD, Caldas C, et al. Liquid biopsies come of age: Towards implementation of circulating tumour DNA. Nat Rev Cancer. 2017;17(4):223-38.
14. Shi J, Kantoff PW, Wooster R, Farokhzad OC. Cancer nanomedicine: Progress, challenges and opportunities. Nat Rev Cancer. 2017;17(1):20-37.
15. Mitchell MJ, Billingsley MM, Haley RM, Wechsler ME, Peppas NA, Langer R. Engineering precision nanoparticles for drug delivery. Nat Rev Drug Discov. 2021;20(2):101-24.
16. Ferrari M. Cancer nanotechnology: Opportunities and challenges. Nat Rev Cancer. 2005;5(3):161-71.
17. Kelkar SS, Reineke TM. Theranostics: Combining imaging and therapy. Bioconjug Chem. 2011;22(10):1879-903.
18. Ventola CL. The nanomedicine revolution: Part 1—Emergence and current status. P T. 2012;37(9):512-25.
19. Barenholz YC. Doxil®—the first FDA-approved nano-drug: Lessons learned. J Control Release. 2012;160(2):117-34.

 doi:10.20944/preprints202510.2360.v2

20. Desai N, Trieu V, Yao Z, Louie L, Ci S, Yang A, et al. Increased antitumor activity, intratumor paclitaxel concentrations, and endothelial cell transport of cremophor-free, albumin-bound paclitaxel (ABI-007) compared with cremophor-based paclitaxel. Clin Cancer Res. 2006;12(4):1317-24.
21. Jokerst JV, Gambhir SS. Molecular imaging with theranostic nanoparticles. Acc Chem Res. 2011;44(10):1050-60.
22. DeVita VT Jr, Lawrence TS, Rosenberg SA. Cancer: Principles & Practice of Oncology. 12th ed. Philadelphia: Wolters Kluwer; 2023.
23. van der Kwast T, Bubendorf L, Moller H. Histopathology in cancer diagnosis: Current challenges and future perspectives. Virchows Arch. 2021;478(3):481-9.
24. Padhani AR, Lecouvet FE, Tunariu N, Koh DM, De Keyzer F, Collins DJ, et al. Imaging cancer treatment response with MRI: Techniques, challenges, and opportunities. Radiology. 2017;282(2):358-75.
25. Hricak H, Leddy R, Sala E, Barentsz J, Reed N. Imaging in oncology: An overview. Cancer Imaging. 2011;11(1A):S1–S12.
26. Roychowdhury S, Chinnaiyan AM. Advancing precision medicine for prostate cancer through genomics. J Clin Oncol. 2013;31(15):1866-73.
27. McGivney WT, Koh WJ, Green S. Surgery in cancer care: Current role and future directions. CA Cancer J Clin. 2018;68(4):261-89.
28. Jaffray DA, Gospodarowicz MK. Radiotherapy for cancer: Present and future. Nat Rev Clin Oncol. 2019;16(12):719-28.
29. Gottesman MM. Mechanisms of cancer drug resistance. Annu Rev Med. 2002;53:615-27.
30. Sharma P, Allison JP. The future of immune checkpoint therapy. Science. 2015;348(6230):56-61.
31. Holohan C, Van Schaeybroeck S, Longley DB, Johnston PG. Cancer drug resistance: An evolving paradigm. Nat Rev Cancer. 2013;13(10):714-26.
32. Longley DB, Johnston PG. Molecular mechanisms of drug resistance. J Pathol. 2005;205(2):275-92.
33. Vasan N, Baselga J, Hyman DM. A view on drug resistance in cancer. Nature. 2019;575(7782):299-309.
34. Bertrand N, Wu J, Xu X, Kamaly N, Farokhzad OC. Cancer nanotechnology: The impact of passive and active targeting in the era of modern cancer biology. Adv Drug Deliv Rev. 2014;66:2-25.
35. Alix-Panabières C, Pantel K. Challenges in circulating tumour cell research. Nat Rev Cancer. 2014;14(9):623-31.
36. Rosenblum D, Joshi N, Tao W, Karp JM, Peer D. Progress and challenges towards targeted delivery of cancer therapeutics. Nat Commun. 2018;9(1):1410.
37. Iqbal N, Iqbal N. Human epidermal growth factor receptor 2 (HER2) in cancers: Overexpression and therapeutic implications. Mol Biol Int. 2014;2014:852748.
38. Xu X, Ho W, Zhang X, Bertrand N, Farokhzad O. Cancer nanomedicine: From targeted delivery to combination therapy. Trends Mol Med. 2015;21(4):223-32.
39. Wicki A, Witzigmann D, Balasubramanian V, Huwyler J. Nanomedicine in cancer therapy: Challenges, opportunities, and clinical applications. J Control Release. 2015;200:138-57.
40. Blanco E, Shen H, Ferrari M. Principles of nanoparticle design for overcoming biological barriers to drug delivery. Nat Biotechnol. 2015;33(9):941-51.
41. Bregoli L, Chiarini F, Gambarelli A, Sighinolfi G, Gatti AM, Santi P, et al. Nanomedicine applied to oncology: The role of nanotoxicology. Biomed Microdevices. 2016;18(1):18.
42. Shi J, Votruba AR, Farokhzad OC, Langer R. Nanotechnology in drug delivery and tissue engineering: From discovery to applications. Nano Lett. 2010;10(9):3223-30.
43. Torchilin VP. Multifunctional, stimuli-sensitive nanoparticulate systems for drug delivery. Nat Rev Drug Discov. 2014;13(11):813-27.
44. Mura S, Nicolas J, Couvreur P. Stimuli-responsive nanocarriers for drug delivery. Nat Mater. 2013;12(11):991-1003.
45. Kumari P, Ghosh B, Biswas S. Nanocarriers for cancer-targeted drug delivery. J Drug Target. 2016;24(3):179-91.
46. Peer D, Karp JM, Hong S, Farokhzad OC, Margalit R, Langer R. Nanocarriers as an emerging platform for cancer therapy. Nat Nanotechnol. 2007;2(12):751-60.

 doi:10.20944/preprints202510.2360.v2

47. Bertrand N, Wu J, Xu X, Kamaly N, Farokhzad OC. Cancer nanotechnology: The impact of passive and active targeting in the era of modern cancer biology. Adv Drug Deliv Rev. 2014;66:2-25.
48. Zhang RX, Wong HL, Xue HY, Eoh JY, Wu XY. Nanomedicine-based targeted chemotherapy: Recent advances in cancer therapy. J Control Release. 2016;240:186-201.
49. Maeda H, Wu J, Sawa T, Matsumura Y, Hori K. Tumor vascular permeability and the EPR effect in macromolecular therapeutics: A review. J Control Release. 2000;65(1-2):271-84.
50. Fang J, Nakamura H, Maeda H. The EPR effect: Unique features of tumor blood vessels for drug delivery, factors involved, and limitations and augmentation of the effect. Adv Drug Deliv Rev. 2011;63(3):136-51.
51. Danhier F. To exploit the tumor microenvironment: Since the EPR effect fails in the clinic, what is the future of nanomedicine? J Control Release. 2016;244(Pt A):108-21.
52. Rosenblum D, Joshi N, Tao W, Karp JM, Peer D. Progress and challenges towards targeted delivery of cancer therapeutics. Nat Commun. 2018;9(1):1410.
53. Mitchell MJ, Jain RK, Langer R. Engineering and physical sciences in oncology: Challenges and opportunities. Nat Rev Cancer. 2017;17(11):659-75.
54. van der Meel R, Lammers T, Hennink WE. Cancer nanomedicines: Oversold or underappreciated? Expert Opin Drug Deliv. 2017;14(1):1-5.
55. Hare JI, Lammers T, Ashford MB, Puri S, Storm G, Barry ST. Challenges and strategies in anti-cancer nanomedicine development: An industry perspective. Adv Drug Deliv Rev. 2017;108:25-38.
56. Petros RA, DeSimone JM. Strategies in the design of nanoparticles for therapeutic applications. Nat Rev Drug Discov. 2010;9(8):615-27.
57. Albanese A, Tang PS, Chan WC. The effect of nanoparticle size, shape, and surface chemistry on biological systems. Annu Rev Biomed Eng. 2012;14:1-16.
58. Salvati A, Pitek AS, Monopoli MP, Prapainop K, Bombelli FB, Hristov DR, et al. Transferrin-functionalized nanoparticles lose their targeting capabilities when a biomolecule corona adsorbs on the surface. Nat Nanotechnol. 2013;8(2):137-43.
59. Blanco E, Shen H, Ferrari M. Principles of nanoparticle design for overcoming biological barriers to drug delivery. Nat Biotechnol. 2015;33(9):941-51.
60. Wilhelm S, Tavares AJ, Dai Q, Ohta S, Audet J, Dvorak HF, et al. Analysis of nanoparticle delivery to tumours. Nat Rev Mater. 2016;1(5):16014.
61. Fang RH, Kroll AV, Gao W, Zhang L. Cell membrane coating nanotechnology. Adv Mater. 2018;30(23):1706759.
62. Fang RH, Hu CMJ, Luk BT, Gao W, Copp JA, Tai Y, et al. Cancer cell membrane-coated nanoparticles for anticancer vaccination and drug delivery. Nano Lett. 2014;14(4):2181-8.
63. Kroll AV, Fang RH, Zhang L. Biointerfacing and applications of cell membrane-coated nanoparticles. Bioconjug Chem. 2017;28(1):23-32.
64. Li SY, Cheng H, Qiu WX, Zhang L, Wan SS, Zeng JY, et al. Cancer cell membrane-coated biomimetic nanoparticles for targeted therapy. Biomaterials. 2017;133:37-48.
65. Li J, Wang Y, Zhu Y, Oupický D. Recent advances in delivery of drug-nucleic acid combinations for cancer treatment. Adv Drug Deliv Rev. 2017;115:33-45.
66. Xu CF, Wang J. Delivery systems for siRNA drug development in cancer therapy. Asian J Pharm Sci. 2015;10(1):1-12.
67. Zhang P, Chen Y, Zeng Y, Shen C, Li R, Guo Z, et al. Targeted delivery of chemotherapeutic agents and genes using ligand-modified nanoparticles for cancer therapy. J Control Release. 2022;343:722-47.
68. Prabhakar U, Maeda H, Jain RK, Sevick-Muraca EM, Zamboni W, Farokhzad OC, et al. Challenges and key considerations of the enhanced permeability and retention (EPR) effect for nanomedicine drug delivery in oncology. Cancer Res. 2013;73(8):2412-7.
69. Wang AZ, Langer R, Farokhzad OC. Nanoparticle delivery of cancer drugs. Annu Rev Med. 2012;63:185-98.
70. Dai Q, Wilhelm S, Ding D, Syed AM, Sindhwani S, Zhang Y, et al. Quantifying the ligand-mediated uptake of nanoparticles in cancer cells. ACS Nano. 2018;12(8):8423-35.

 doi:10.20944/preprints202510.2360.v2

71. Miao L, Lin CM, Huang L. Cancer nanomedicine: From targeted delivery to combination therapy. Trends Pharmacol Sci. 2015;36(9):789-801.
72. Lee Y, Thompson DH. Stimuli-responsive liposomes for drug delivery. Wiley Interdiscip Rev Nanomed Nanobiotechnol. 2017;9(5):e1450.
73. Torchilin VP. Recent advances with liposomes as pharmaceutical carriers. Nat Rev Drug Discov. 2005;4(2):145-60.
74. Wang H, Agarwal P, Zhao S, Xu RX, Yu J, Lu X, et al. Combined cancer therapy with hyaluronic acid-based nanomaterials. Biomaterials. 2018;180:12-24.
75. Zhang X, Li C, Wang L, Zhang J, Chen Y, Dong J, et al. Multifunctional nanocarriers for stimuli-responsive drug delivery in cancer therapy. Chem Soc Rev. 2022;51(5):1704-36.
76. Liu Y, Crawford BM, Vo-Dinh T. Gold nanoparticles for drug delivery and cancer therapy. Nanomedicine (Lond). 2021;16(3):123-43.
77. Tang L, Cheng J. Nonporous silica nanoparticles for nanomedicine application. Nano Today. 2013;8(3):290–312.
78. Anselmo AC, Mitragotri S. Nanoparticles in the clinic: An update post COVID-19 vaccines. Bioeng Transl Med. 2021;6(3):e10246.
79. Chen G, Roy I, Yang C, Prasad PN. Nanochemistry and nanomedicine for nanoparticle-based diagnostics and therapy. Chem Rev. 2016;116(5):2826–85.
80. Dreaden EC, Austin LA, Mackey MA, El-Sayed MA. Size matters: Gold nanoparticles in targeted cancer drug delivery. Ther Deliv. 2012;3(4):457–78.
81. Alexis F, Pridgen E, Molnar LK, Farokhzad OC. Factors affecting the clearance and biodistribution of polymeric nanoparticles. Mol Pharm. 2008;5(4):505–15.
82. Kamaly N, Yameen B, Wu J, Farokhzad OC. Degradable controlled-release polymers and polymeric nanoparticles: Mechanisms of controlling drug release. Chem Rev. 2016;116(4):2602–63.
83. Duncan R, Gaspar R. Nanomedicine(s) under the microscope. Mol Pharm. 2011;8(6):2101–41.
84. Ma X, Williams RO III. Polymeric nanomedicines for poorly soluble drugs in cancer therapy. J Pharm Sci. 2018;107(1):10–24.
85. Makadia HK, Siegel SJ. Poly lactic-co-glycolic acid (PLGA) as biodegradable controlled drug delivery carrier. Polymers (Basel). 2011;3(3):1377–97.
86. Avgoustakis K. Pegylated poly(lactide) and poly(lactide-co-glycolide) nanoparticles: Preparation, properties and possible applications in drug delivery. Curr Drug Deliv. 2004;1(4):321–33.
87. Danhier F, Ansorena E, Silva JM, Coco R, Le Breton A, Préat V. PLGA-based nanoparticles: An overview of biomedical applications. J Control Release. 2012;161(2):505–22.
88. Yoo J, Park C, Yi G, Lee D, Koo H. Active targeting strategies using biological ligands for nanoparticle drug delivery systems. Cancers (Basel). 2019;11(5):640.
89. Fang RH, Kroll AV, Gao W, Zhang L. Cell membrane coating nanotechnology. Adv Mater. 2018;30(23):1706759.
90. Luk BT, Zhang L. Cell membrane-camouflaged nanoparticles for drug delivery. J Control Release. 2015;220(Pt B):600–7.
91. Zhang L, Chan JM, Gu FX, Rhee JW, Wang AZ, Radovic-Moreno AF, et al. Self-assembled lipid–polymer hybrid nanoparticles: A robust drug delivery platform. ACS Nano. 2008;2(8):1696–702.
92. Parodi A, Quattrocchi N, van de Ven AL, Chiappini C, Evangelopoulos M, Martinez JO, et al. Synthetic nanoparticles functionalized with biomimetic leukocyte membranes possess cell-like functions. Nat Nanotechnol. 2013;8(1):61–8.
93. Hu CMJ, Zhang L, Aryal S, Cheung C, Fang RH, Zhang L. Erythrocyte membrane-camouflaged polymeric nanoparticles as a biomimetic delivery platform. Proc Natl Acad Sci U S A. 2011;108(27):10980–5.
94. Li R, He Y, Zhu Y, Jiang L, Zhang S, Qin J, et al. Route to multifunctional biomimetic nanoparticles in biomedical applications. Adv Mater. 2019;31(8):1804828.
95. Zhang Q, Dehaini D, Zhang Y, Zhou J, Chen X, Zhang L, et al. Neutrophil membrane-coated nanoparticles inhibit synovial inflammation and alleviate joint damage in inflammatory arthritis. Nat Nanotechnol. 2018;13(12):1182–90.

 doi:10.20944/preprints202510.2360.v2

96. Meng QF, Rao L, Zan M, Chen M, Yu GT, Wei X, et al. Biomimetic immunomagnetic nanoparticles for theranostic applications in leukemia. Adv Mater. 2020;32(18):1907461.
97. Zhen X, Cheng P, Pu K. Recent advances in cell membrane–camouflaged nanoparticles for cancer phototheranostics. Small. 2019;15(12):1804105.
98. Sun H, Su J, Meng Q, Yin Q, Chen L, Gu W, et al. Cancer-cell-biomimetic nanoparticles for targeted therapy of homotypic tumors. Adv Mater. 2016;28(43):9581–8.
99. Yang R, Xu J, Xu L, Sun X, Chen Q, Zhao Y, et al. Cancer cell membrane-coated adjuvant nanoparticles with mannose modification for effective anticancer vaccination. ACS Nano. 2018;12(6):5121–9.
100. Luo M, Wang H, Wang Z, Cai H, Lu Z, Li Y, et al. A STING-activating nanovaccine for cancer immunotherapy. Nat Nanotechnol. 2017;12(7):648–54.
101. Hu CMJ, Fang RH, Luk BT, Zhang L. Polymeric nanotherapeutics: Clinical development and advances in stealth functionalization strategies. Nanoscale. 2014;6(1):65–75.
102. Guo Y, Wang D, Song Q, Wu T, Zhuang X, Bao Y, et al. Erythrocyte membrane-enveloped polymeric nanoparticles as nanovaccine for influenza virus. ACS Nano. 2015;9(7):6918–33.
103. Molinaro R, Corbo C, Martinez JO, Taraballi F, Evangelopoulos M, Minardi S, et al. Biomimetic proteolipid vesicles for targeting inflamed tissues. Nat Mater. 2016;15(9):1037–46.
104. Suk JS, Xu Q, Kim N, Hanes J, Ensign LM. PEGylation as a strategy for improving nanoparticle-based drug and gene delivery. Adv Drug Deliv Rev. 2016;99(Pt A):28–51.
105. Barenholz YC. Doxil®—the first FDA-approved nano-drug: lessons learned. J Control Release. 2012;160(2):117–34.
106. Allen TM, Cullis PR. Liposomal drug delivery systems: from concept to clinical applications. Adv Drug Deliv Rev. 2013;65(1):36–48.
107. Silverman JA, Deitcher SR. Marqibo® (vincristine sulfate liposome injection) improves the pharmacokinetics and pharmacodynamics of vincristine. Cancer Chemother Pharmacol. 2013;71(3):555–64.
108. Sofou S. Liposomal nanocarriers in cancer therapy: from preclinical to clinical progress. Adv Drug Deliv Rev. 2021;179:113912.
109. Bobo D, Robinson KJ, Islam J, Thurecht KJ, Corrie SR. Nanoparticle-based medicines: a review of FDA-approved materials and clinical trials to date. Pharm Res. 2016;33(10):2373–87.
110. Ventola CL. Progress in nanomedicine: approved and investigational nanodrugs. P T. 2017;42(12):742–55.
111. Etheridge ML, Campbell SA, Erdman AG, Haynes CL, Wolf SM, McCullough J. The big picture on nanomedicine: the state of investigational and approved nanomedicine products. Nanomedicine. 2013;9(1):1–14.
112. Park K. The beginning of the end of the nanomedicine hype. J Control Release. 2019;305:221–2.
113. Shi J, Kantoff PW, Wooster R, Farokhzad OC. Cancer nanomedicine: progress, challenges and opportunities. Nat Rev Cancer. 2017;17(1):20–37.
114. Xu X, Ho W, Zhang X, Bertrand N, Farokhzad OC. Cancer nanomedicine: from targeted delivery to combination therapy. Trends Mol Med. 2015;21(4):223–32.
115. Anselmo AC, Mitragotri S. Nanoparticles in the clinic: An update post COVID-19 vaccines. Bioeng Transl Med. 2021;6(3):e10246.
116. Wicki A, Witzigmann D, Balasubramanian V, Huwyler J. Nanomedicine in cancer therapy: challenges, opportunities, and clinical applications. J Control Release. 2015;200:138–57.
117. Rosenblum D, Joshi N, Tao W, Karp JM, Peer D. Progress and challenges towards targeted delivery of cancer therapeutics. Nat Commun. 2018;9:1410.
118. Zamboni WC, Torchilin V, Patri AK, Hrkach J, Stern S, Lee R, et al. Best practices in cancer nanotechnology: perspective from NCI nanotechnology alliance. Clin Cancer Res. 2012;18(12):3229–41.
119. Wilhelm S, Tavares AJ, Dai Q, Ohta S, Audet J, Dvorak HF, Chan WCW. Analysis of nanoparticle delivery to tumours. Nat Rev Mater. 2016;1(5):16014.
120. Hare J, Lammers T, Ashford M, Puri S, Storm G, Barry S. Challenges and strategies in anti-cancer nanomedicine translation. Nat Rev Clin Oncol. 2017;14(12):731–46.
121. Bobo D, Corrie SR, Thurecht KJ. Nanoparticles in clinical trials: current status and future perspectives. Nanomedicine. 2020;15(11):1073–84.

 doi:10.20944/preprints202510.2360.v2

122. ClinicalTrials.gov. Clinical trials involving nanomedicines in oncology. [Internet]. Bethesda (MD): National Library of Medicine; updated 2025 [cited 2025 Oct 29]. Available from: https://clinicaltrials.gov
123. Wilhelm S, Tavares AJ, Dai Q, Ohta S, Audet J, Dvorak HF, Chan WCW. Analysis of nanoparticle delivery to tumours. Nat Rev Mater. 2016;1(5):16014.
124. Blanco E, Shen H, Ferrari M. Principles of nanoparticle design for overcoming biological barriers to drug delivery. Nat Biotechnol. 2015;33(9):941–51.
125. Venditto VJ, Szoka FC Jr. Cancer nanomedicines: so many papers and so few drugs! Adv Drug Deliv Rev. 2013;65(1):80–8.
126. Hare J, Lammers T, Ashford M, Puri S, Storm G, Barry S. Challenges and strategies in anti-cancer nanomedicine translation. Nat Rev Clin Oncol. 2017;14(12):731–46.
127. Kunjachan S, Ehling J, Storm G, Kiessling F, Lammers T. Noninvasive imaging of nanomedicines and nanotheranostics: principles, progress, and prospects. Chem Rev. 2015;115(19):10907–37.
128. Moghimi SM, Simberg D. Nanoparticle clearance pathways and toxicity. Toxicol Appl Pharmacol. 2018;360:264–8.
129. Nel AE, Madler L, Velegol D, Xia T, Hoek EM, Somasundaran P, et al. Understanding biophysicochemical interactions at the nano–bio interface. Nat Mater. 2009;8(7):543–57.
130. Alexis F, Pridgen E, Molnar LK, Farokhzad OC. Factors affecting the clearance and biodistribution of polymeric nanoparticles. Mol Pharm. 2008;5(4):505–15.
131. Chan WCW. Nanomedicine 2.0. Acc Chem Res. 2017;50(3):627–32.
132. Torrice M. Does nanomedicine have a delivery problem? ACS Cent Sci. 2016;2(7):434–7.
133. Docter D, Strieth S, Westmeier D, Hayden O, Gao M, Knauer SK, Stauber RH. No king without a crown—impact of the protein corona on nanoparticle interactions in vitro and in vivo. Nanomedicine. 2015;10(12):3121–38.
134. Albanese A, Tang PS, Chan WCW. The effect of nanoparticle size, shape, and surface chemistry on biological systems. Annu Rev Biomed Eng. 2012;14:1–16.
135. Maeda H, Khatami M. Analyses of repeated failures in cancer nanomedicine: a call for new strategies. Cancer Sci. 2018;109(4):959–68.
136. Shi Y, van der Meel R, Chen X, Lammers T. The EPR effect and beyond: strategies to improve tumour targeting and cancer nanomedicine efficacy. Theranostics. 2020;10(17):7921–4.
137. Tinkle S, McNeil SE, Mühlebach S, Bawa R, Borchard G, Barenholz Y, et al. Nanomedicines: addressing the scientific and regulatory gap. Ann N Y Acad Sci. 2014;1313(1):35–56.
138. Park K. Facing the truth about nanomedicine: the lessons from COVID-19 vaccines. J Control Release. 2021;335:253–6.
139. Wicki A, Witzigmann D, Balasubramanian V, Huwyler J. Nanomedicine in cancer therapy: challenges, opportunities, and clinical applications. J Control Release. 2015;200:138–57.
140. Etheridge ML, Campbell SA, Erdman AG, Haynes CL, Wolf SM, McCullough J. The big picture on nanomedicine: the state of investigational and approved nanomedicine products. Nanomedicine. 2013;9(1):1–14.
141. Yu M, Zheng J. Clearance pathways and tumor targeting of imaging nanoparticles. ACS Nano. 2015;9(7):6655–74.
142. Pettersson M, Crews CM. PROteolysis TArgeting Chimeras (PROTACs)—past, present and future. Drug Discov Today Technol. 2019;31:15–27.
143. Burslem GM, Crews CM. Proteolysis-targeting chimeras as therapeutics and tools for biological discovery. Cell. 2020;181(1):102–14.
144. Lai AC, Crews CM. Induced protein degradation: an emerging drug discovery paradigm. Nat Rev Drug Discov. 2017;16(2):101–14.
145. Sun X, Gao H, Yang Y, He M, Wu Y, Song Y, et al. PROTACs: great opportunities for academia and industry. Signal Transduct Target Ther. 2019;4:64.
146. Neklesa TK, Winkler JD, Crews CM. Targeted protein degradation by PROTACs: applications and challenges. Pharmacol Ther. 2017;174:138–44.

 doi:10.20944/preprints202510.2360.v2

147. Paiva S-L, Crews CM. Targeted protein degradation: elements of PROTAC design. Curr Opin Chem Biol. 2019;50:111–9.
148. Wang C, Zhang Y, Chen Y, Xu Y, Ma L, Zhang Q. Nanocarrier-based PROTAC delivery for cancer therapy. Adv Drug Deliv Rev. 2023;199:114918.
149. Liu J, Chen H, Ma L, Dang Y, Li X, Zhou C, et al. Integration of PROTAC technology with nanomedicine for precise tumor therapy. Nano Today. 2024;54:102096.
150. Riley RS, June CH, Langer R, Mitchell MJ. Delivery technologies for cancer immunotherapy. Nat Rev Drug Discov. 2019;18(3):175–96.
151. Zhang Y, Shi J, Zhang H, Xu Q, Chen X. Immuno-nanomedicine for cancer therapy: recent advances and future prospects. Chem Soc Rev. 2022;51(17):7285–316.
152. Hu Q, Li H, Archibong E, Chen Q, Wang C, Xu H, et al. In situ administration of nanomedicine for tumor immunotherapy. Nat Nanotechnol. 2021;16(4):410–20.
153. Koshy ST, Mooney DJ. Biomaterials for enhancing anti-cancer immunity. Nat Rev Cancer. 2016;16(3):159–70.
154. Ghosh S, Thakur A, Maiti TK. Personalized nanomedicine: opportunities and challenges for precision oncology. Adv Drug Deliv Rev. 2023;198:114887.
155. Zhang X, Liu Y, Fan Z, Zhang H. Hybrid nanostructures for multimodal cancer therapy. Adv Mater. 2020;32(31):2001071.
156. He H, Liu L, Morin EE, Liu M, Schwendeman A. Survey of clinical translation of cancer nanomedicines—lessons learned and future directions. J Control Release. 2020;319:407–20.
157. Wicki A, Lammers T. Nanomedicine for future precision cancer therapy: opportunities and obstacles. Adv Drug Deliv Rev. 2024;205:114996.
158. Mitchell MJ, Billingsley MM, Haley RM, Wechsler ME, Peppas NA, Langer R. Engineering precision nanoparticles for drug delivery. Nat Rev Drug Discov. 2021;20(2):101–24.