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(REVIEW ARTICLE)

EMERGING NANOMEDICINE STRATEGIES FOR PRECISION CANCER THERAPY

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ABSTRACT

Cancer remains a major global health challenge, necessitating the development of innovative therapeutic approaches that improve treatment efficacy while minimizing adverse effects on healthy tissues. Nanomedicine has emerged as a promising strategy for precision cancer therapy by enabling targeted drug delivery, controlled drug release, and enhanced therapeutic selectivity. This review explores recent advances in nanomedicine platforms, including liposomes, polymeric nanoparticles, lipid-based nanocarriers, metallic nanoparticles, dendrimers, and biomimetic nanocarriers, for the diagnosis and treatment of cancer. These nanocarriers can be engineered to improve drug solubility, stability, bioavailability, and accumulation within tumor tissues. Furthermore, multifunctional nanoplatforms have demonstrated potential in integrating chemotherapy, photothermal therapy, photodynamic therapy, gene therapy, and immunotherapy to achieve synergistic anticancer effects. Emerging approaches involving artificial intelligence, biomimetic materials, and personalized nanomedicine may further support the development of patient-specific treatment strategies based on tumor molecular characteristics. Despite these advances, several challenges remain, including biological barriers to drug delivery, heterogeneous tumor microenvironments, nanoparticle toxicity, immune responses, manufacturing complexity, and regulatory requirements. Addressing these limitations through rational nanocarrier design, comprehensive preclinical evaluation, and well-designed clinical studies is essential for translating promising laboratory findings into effective cancer treatments. Overall, emerging nanomedicine strategies offer considerable potential to advance precision oncology by improving therapeutic targeting, optimizing treatment outcomes, and supporting individualized cancer management. Continued interdisciplinary research and clinical

validation will be critical to establishing safe, effective, and accessible nanomedicine-based therapies for diverse cancer types.

Keywords: Cancer, Nanomedicine, Active and Passive Targeting, Chemotherapy

1 INTRODUCTION

Cancer is a type of tumor that demonstrates abnormal cell growth with the potential to invade or spread from its originating organ ("site") to other parts of the body. Tumors gain their potential to invade or spread by acquiring multiple malignant phenotypes through genetic and epigenetic alterations that disrupt key cellular pathways such as DNA damage and repair, control of proliferation, and avoiding immune destruction.[1]

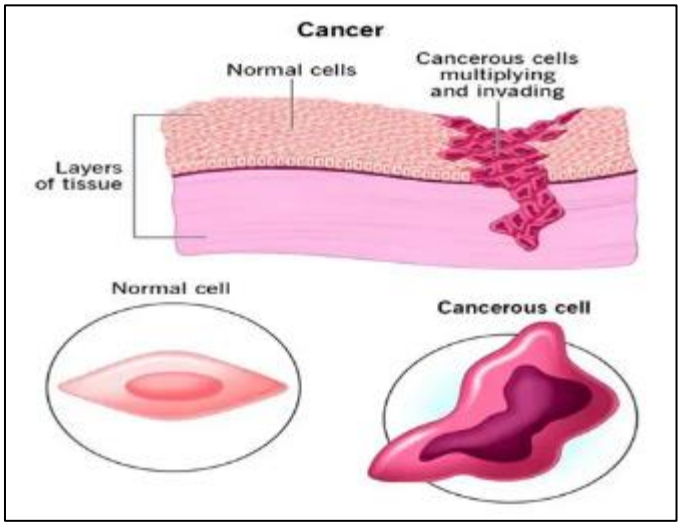


Figure 1: Cancer cell

1.1 Causes

- Epidemiologic studies have identified associations between many characteristics and cancer risk. For some characteristics, clear-cut causal associations have been established.
- Cigarette smoking causes 13 different malignancies: cancers of the lung, oral cavity, larynx, esophagus, bladder, kidney, pancreas, stomach, cervix, colon, rectum, and liver and acute myelogenous leukemia. An estimated 48% of all deaths resulting from cancer in the United States are attributable to cigarette smoking. Other forms of tobacco use, including smoking pipes and cigars, and chewing tobacco, as well as second-hand exposure to tobacco smoke, cause cancer in a more limited number of organs.[2,3,4]
- Exposure to 2 forms of radiation causes cancer. Ionizing radiation is an established cause of leukemia, thyroid cancer, and female breast cancer. Exposure to UVR, either from sunlight or from indoor tanning devices, is a major cause of melanoma and nonmelanoma skin cancers.[4,5]
- Infectious agents cause 18% of all cancers worldwide, with greater importance in lower-income compared to higher-income countries. The most important cancer-causing infectious agents are oncogenic strains of HPV (cancers of the cervix, vulva, vagina, anus, penis), hepatitis B and C viruses (liver cancer), Epstein–Barr virus (EBV; Burkitt lymphoma), and Helicobactor pylori (gastric cancer).[4,6,7]
- Drinking alcohol causes liver, colorectal (men), breast (women), oral cavity, and squamous cell esophageal cancers.[8]
- The potential contribution of diet and physical activity to cancer risk has also been intensively researched. The World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) continuous update project report assessed the overall evidence of diet in relation to cancer prevention. The evidence for each dietary factor in relation to cancer was evaluated and rated as either "strong" or "limited," and strong evidence was further rated as "convincing" or "probable." Aside from alcohol (noted above), the only convincingly strong evidence for increased risk is obesity (operationalized as body mass index, or BMI). BMI is convincingly positively associated with 7 cancers (esophageal adenocarcinoma, pancreas, liver, colorectum, post-menopausal breast, endometrium, and kidney), and probably positively associated with 5 cancers (mouth/pharynx/larynx, stomach, gallbladder, ovary, and prostate). The WCRF/AICR report found that increasing physical activity is convincingly associated with a reduced risk of colorectal cancer and probably associated with a reduced risk of post-menopausal breast cancer and endometrial cancer.[9,10]

- Depending on their formulation, steroid hormone medications are both risk and protective factors for breast, endometrial, and ovarian cancer. Hormone replacement therapy (i.e., unopposed estrogens) causes endometrial and ovarian cancers. Menopausal hormone therapy (i.e., estrogen and progesterone) is a cause of breast cancer but prevents endometrial cancer. In contrast, oral contraceptives containing primarily progestins (irrespective of their estrogen content) protect against the development of endometrial and ovarian cancer.[11]
- A person's occupation was one of the earliest cancer risk factors to be identified when in 1775 English surgeon Percivall Pott reported an increased risk of scrotal carcinomas in young boys who worked as chimney sweeps. Most occupations that are causes of cancer are activities that involve exposure to chemicals, such as organic solvents, known to exert damaging effects on cellular DNA. Formal assessments suggest that 2% to 8% of cancers in the general population can be attributed to occupational causes, with the proportion being higher among men than women.[12]

1.2 Pathophysiology

A majority of cancers contain activating mutations or chromosomal rearrangements in genes—dubbed oncogenes—that serve to chronically sustain otherwise transitory cell proliferation via triggering and stimulating progression through the cell division cycle. Most prominent is KRAS, which—via activating point mutations—upregulates a complex intracellular signaling network that, among other things, drives chronic proliferation. KRAS is mutated in ~30% of human tumors, including pancreatic adenocarcinoma (90%), colorectal cancer (50%), and lung adenocarcinoma (35%). Beyond KRAS and its homologs NRAS and HRAS, other commonly mutated proliferation-inducing "driver" oncogenes include PIK3CA, BRAF, and BCR-ABL. Other genes can become oncogenes by virtue of gene amplifications and other rearrangements, including often-circular extrachromosomal DNA elements (ecDNA), which collectively serve to induce/overexpress wild-type growth-stimulating proteins. Examples include MYC, CCND1, EGFR, and EGFR2/HER2, although the latter two can also be mutationally activated in certain cancer types. Most notably, the MYC gene, encoding a heterodimeric transcription factor (TF) that regulates thousands of genes, is amplified/rearranged, or its antagonists deleted, in 40% of human tumors. Other tumors lacking structural changes in the MYC gene locus have evidence for increased MYC expression and transcriptional activity by upregulation of its expression or post-translational modifications. Currently, 193 genes have been defined as proliferation-driving oncogenes by virtue of mutational alteration in human tumors and functional validation in model systems. The precise mechanistic contributions of these non-canonical mutant genes to this and other hallmark capabilities are diverse and the subject of continuing investigation.[13-15]

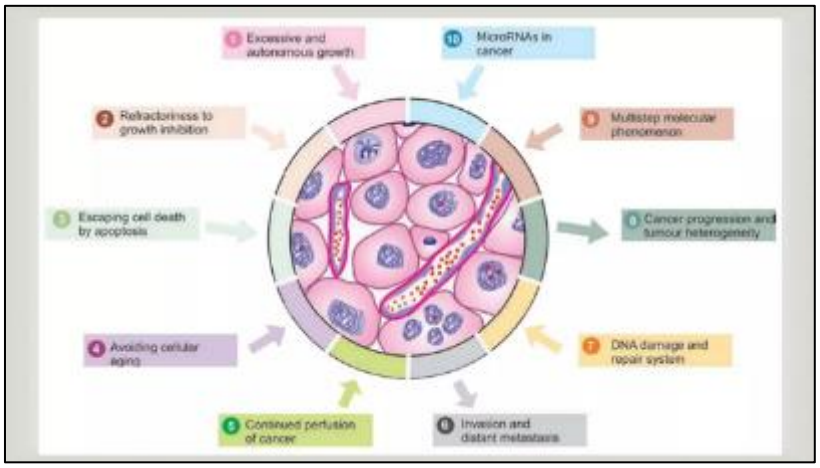


Figure 2: Stages of cancer development

2 NANOMEDICINE IN CLINICAL CANCER CARE

Various types of nanomedicine compounds have been used in clinical cancer care, including viral vectors, drug conjugates, lipid-based nanocarriers, polymer-based nanocarriers, and inorganic nanoparticles. Most nanomedicine therapeutics are investigated in phase 1 trials in patients with solid tumors. Specific cancer indications are explored in advanced (phases 2 and 3).[16]

2.1 Mechanisms of Nanoparticle-Mediated Drug Delivery

2.1.1 Passive Targeting

Tumor vasculature, marked by a high ratio of proliferating endothelial cells and swift angiogenesis, exhibits unique pathophysiological traits. The rapid expansion of tumor tissues prompts irregularities in cell architecture, such as an

increased cell curvature, insufficient neovascular outer membrane cells, and basement membrane deformation. Together with poor lymphatic reflux in tumor tissues, these irregularities foster the accumulation of NPs that penetrate through tumor capillary "gaps" and infiltrate tumor tissues—a phenomenon known as the "enhanced permeation and retention (EPR) effect". The EPR effect forms the foundation for passive targeting, a key mechanism for the tumor accumulation of prospective nanocarriers.[17]

The effects of nanomedicine within the body are considerably influenced by particle size. For instance, NPs of less than 5 nm are susceptible to quick renal filtration due to their hydrophilic nature. In comparison, NPs exceeding 200 nm often accumulate rapidly in healthy organs or are swiftly absorbed by macrophages. Nanocarriers with particle sizes ranging between 5 and 250 nm can infiltrate leaking tumor vessels and accumulate effectively over time, given the absence of functional lymphatic drainage in tumor tissues. Surface properties, such as charge and hydrophobicity, are vital in influencing protein photochemical changes and cellular uptake rates. Unlike hydrophobic and positively charged particles, neutral or negatively charged and hydrophilic particles demonstrate lower non-specific internalization rates and shorter in vivo circulating half-lives. Stability, another key determinant of NPs' circulation duration, is equally critical for efficient tumor targeting. Studies have shown that drug leakage from stable NPs often occurs before they reach their target, rendering premature drug release a significant factor impacting tumor targeting efficiency. The efficacy of passive targeting relies on tumor biology, including factors such as the extent of vascular and lymphatic vessel generation, perivascular tumor invasion, and intra-tumor pressure. These elements, along with the physicochemical properties of NPs, determine the efficiency of passive nanomedicine targeting. In addition, the efficiency of targeting heavily relies on blood circulation time. Indeed, for systemically administered nanomaterials intended as drug delivery systems, kinetically slow transportation into the diseased tissues due to vascular barriers necessitates a relatively longer circulation time to increase the chance of crossing the vascular wall. One of the critical hindrances to prolonged blood circulation is the rapid clearance ofnanomedicine by the reticuloendothelial system (RES).[18,19]

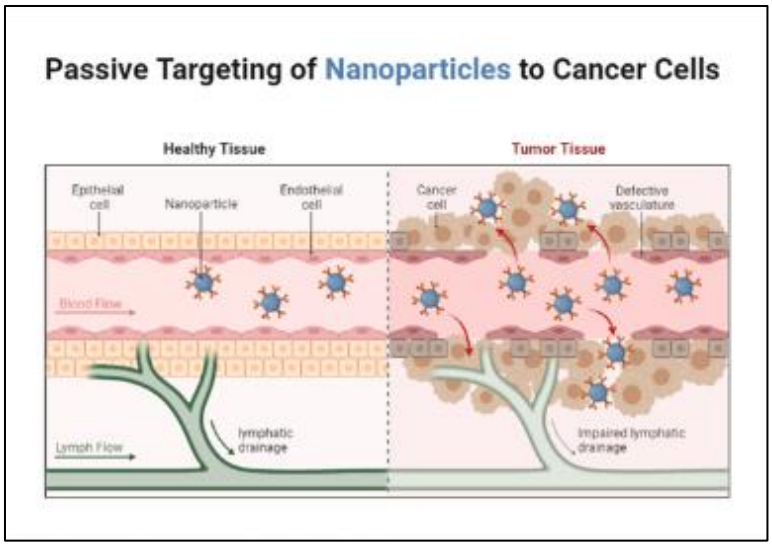


Figure 3: Passive targeting of cancer cells

To counteract this issue, steric stabilization techniques, such as PEGylation, have been introduced. This method exploits the principle of steric repulsion to retard RES clearance and prolong circulation. For example, the nanotechnology field leverages PEG to create 'stealth' drug carriers granting prolonged circulation times and decreased recognition and clearance by the mononuclear phagocyte system (MPS). Today, most nanomedicines approved for clinical use contain PEG, and it has been instrumental in recent advancements, such as the two mRNA-based COVID-19 vaccines, which are delivered by PEGylated lipid nanoparticles. However, despite its pervasive use, it has become clear that PEG is not as immunologically inert as initially thought. Some studies increasingly indicate that the repeated systemic injection of PEGylated drugs can trigger immunogenic responses, which may result in hypersensitivity reactions and compromised therapeutic efficacy. Furthermore, anti-PEG antibodies have been detected in healthy individuals who have not previously received PEGylated drugs, hinting at a complex immunological landscape yet to be fully understood. Recent studies have unveiled the intergenerational inheritance of anti-PEG antibodies, shedding light on the potential long-term ramifications of PEGylated nanomedicines. In addition, high titers of anti-PEG antibodies have been associated with adverse events, such as non-infectious fever after the administration of PEGylated therapeutics, and shown to interact with PEGylated liposomes. Given the above circumstances, the clinical use of PEG-conjugated therapeutics has been impeded by its immunogenicity. A novel approach mitigates this issue by incorporating gangliosides into PEGylated liposomes, significantly reducing the production of anti-PEG IgM and subsequent rapid clearance of the drug. This strategy promises to sustain the therapeutic efficacy of PEGylated liposomes, particularly upon repeated

administration. Thus, researchers are currently exploring novel alternatives to address these emerging challenges. Such alternatives offer a promising pathway toward minimizing the immunogenicity of nanoparticle-mediated drug delivery, thereby enhancing their therapeutic potential.[20-22]

2.1.2 Active Targeting

An important subtype of active targeting, cell targeting, is an emerging field in nanomedicine. Targeting specific cells such as cancer cells, immune cells, or even stem cells can potentially improve treatment outcomes in various diseases. This approach involves the design of NPs with specific ligands that can recognize and bind to receptors unique to the target cells. A vital component of this strategy is the ligand-mediated recognition of the target substrate receptor. Interactions between the ligand and target can induce intramembrane folding, leading to NP internalization via receptor-mediated endocytosis. Following internalization, endogenous particles are transported to the nuclear endosome, where further particle processing and drug release occur. This cell-specific delivery can improve therapeutic efficiency and reduce side effects by ensuring that the drugs primarily affect the cells of interest. Numerous studies underline the potential of cell targeting, showcasing a significant enhancement in cellular NP uptake in vitro.[23]

For example, anti-HER2 monoclonal antibody-modified, actively targeted magnetic NPs produced 10–30-foldhigher tumor tissue concentrations than did their non-targeted counterparts. Similar results were observed with folic acid-modified layered double hydroxides and paclitaxel-loaded nanocarriers. By selectively targeting cancer cells and cells adjacent to tumor blood vessels (such as angiogenic endothelial cells), cell targeting can disrupt the blood supply to cancer cells, instigating hypoxia and necrosis. Moreover, this strategy can augment the efficacy of nanocarriers bearing conventional chemotherapeutic drugs. However, the NPs designed for cell targeting must satisfy the prerequisites for passive targeting, including having a suitable particle size, adequate stability, prolonged blood circulation, and efficient drug retention.[24,25]

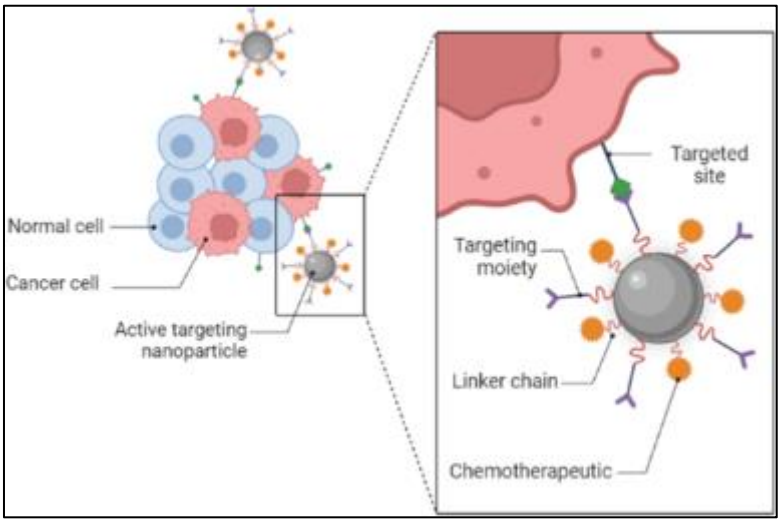


Figure 4: Active targeting of cancer cells

However, cell targeting is not without its challenges. The complexity of biological systems poses significant hurdles. Upon administration into biological fluids, nanocarriers attract proteins onto their surfaces, forming an adsorption layer called the protein corona. This protein layer significantly influences the biological behavior of nanocarriers by altering their physicochemical properties and can ultimately control their in vivo fate. This process significantly impacts nanocarriers' stability, targeting capacity, pharmacokinetics, and toxicity. Therefore, the physiological function of nanoparticles heavily depends on the characterization of the proteins forming the corona. Moreover, protein corona is a Janus-like entity that can positively and negatively impact NP-based therapeutics. On the one hand, protein corona can influence blood circulation, accumulation and penetration at targeting sites, cellular uptake in tumor-targeting delivery, and interactions between NPs and immune cells for immunotherapy. On the other hand, protein corona can also cause unpredictable in vivo behaviors due to the absorption of biomolecules on NPs. For instance, protein corona can reduce the interactions between NPs and the cell membrane by covering the initially modified ligands or presenting an unfavorable steric effect, which decreases cellular uptake. In summary, an in-depth understanding of protein corona and its complex interactions with NPs is essential in designing effective nanocarrier systems for therapeutic deliver. [26,27]

Another significant component of active targeting, known as transcytosis nanomedicine, warrants our attention. In contrast to the classical active targeting mechanism, which predominantly involves the binding of nanomedicine to cell surface receptors, transcytosis nanomedicine takes a step further. It is designed to be transported across cells, exploiting cellular machinery to transport nanomedicine from one side of the cell to the other. This process is beneficial in crossing

biological barriers that are otherwise hard to penetrate, such as the blood–brain barrier or that of specific dense tumoral tissues.[28] The application of transcytosis nanomedicine becomes especially significant in cancer therapy, where the tumor microenvironment (TME) often presents a formidable challenge to conventional drug delivery methods. By utilizing transcytosis nanomedicine, we can enhance the accumulation of therapeutic agents in tumor tissues, improving the efficacy of the treatment while minimizing systemic toxicity. Several strategies can be employed to design transcytosable nanomedicines, including the use of targeting ligands that bind to specific cell-surface receptors triggering endocytosis and the design of nanocarriers that can escape endosomal entrapment to reach the cytosol, promoting exocytosis on the other side of the cell. Furthermore, they can also be engineered to be responsive to various stimuli present in the TME, thereby enhancing their transcytosis efficiency.[29] To fully leverage the potential of transcytosis nanomedicine, ongoing research efforts are dedicated to understanding the molecular mechanisms underlying transcytosis and devising more efficient and specific nanocarrier systems. However, the complexity of transcytosis, combined with the heterogeneity of TME, necessitates a careful and nuanced approach to designing and applying these nanomedicines.[30]

2.1.3 Drug Release

Following the internalization of the nanomedicine, they are transported to the nuclear endosome for further processing and drug release. This process involves the disassembly or degradation of the nanocarrier and the subsequent release of the encapsulated therapeutic agent. The release mechanism can be either passive, which depends on the diffusion or dissolution of the drug, or active, which is triggered by specific stimuli within the cellular or TME.[30,31]

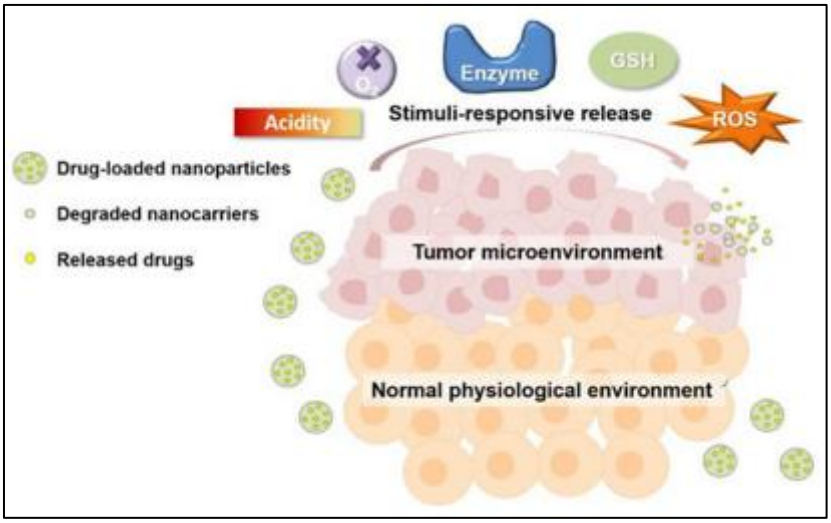


Figure 5: Drug release by cancer nanomedicine

In addition to the findings already outlined in our paper, several relevant studies in the stimuli-responsive nanomedicine field should be considered. Stimuli-responsive nanomedicines represent an innovative approach towards enhancing drug delivery efficiency, characterized by the capacity to respond to specific physical or biological triggers and subsequently control drug release profiles spatially, temporally, and in terms of dosage. External stimuli such as temperature, ultrasound, light, and magnetic fields, as well as internal factors, including pH, redox reactions, and enzyme activation can be employed to trigger the release of drugs loaded in NPs. As elucidated by Mura et al., these systems have the potential to regulate drug biodistribution and improve targeted delivery to diseased areas, thereby addressing the challenge of non-specific cell and tissue biodistribution that often alters drug efficacy. These nanoreactors remain inactive in normal tissues but are activated by the acidic TME, triggering the release of reactive species to induce oxidative stress and suppress the antioxidant abilities of cancer cells, thus leading to synergistic tumor ablation. A study worked on thermoresponsive liposomes for enhanced anti-cancer efficacy. They observed the more significant cytotoxicity of cisplatin-loaded thermoresponsive liposomes at higher temperatures, aligning with the elevated temperature at tumor sites. In recent research, a method was developed using temozolomide-loaded magnetic nanoparticles combined with an alternating magnetic field, significantly suppressing tumor growth and increasing survival rates. In addition, research on pH-responsive nanoparticles has showcased significant progress in cancer treatment. Swetha et al. and Francesco et al. demonstrated the effectiveness of pH-responsive nanovesicles in drug delivery, especially when loaded with doxorubicin, for potent in vivo and in vitro anti-cancer activity. Marianecci et al. highlighted the importance of surfactants in modulating the pH sensitivity of niosomes, a type of colloidal nanocarrier. Furthermore, the unique ROS-responsive nanomedicine platform has been developed by Li et al. to leverage the elevated ROS levels characteristic of tumors, providing a dual action of oxidative stress-induced apoptosis and chemotherapy for synergistic cancer treatment. Lastly, the exploitation of enzymes in the TME has been successfully demonstrated in the design of enzymatically transformable polymer-based nanotherapeutics. The overactivation of matrix

metalloproteinases (MMPs) in tumor-associated tissues catalyzes the transformation of these nanotherapeutics, improving their tissue targeting, retention, and bioavailability while synchronously delivering anti-cancer agents to inhibit malignant progression [52]. Taken together, these studies further support the promising potential of stimuli-responsive nanomedicine in cancer therapy.[32,33]

2.2 The Promising Role of Nanomedicine in Tumor Therapies

The remarkable properties and capabilities of nanomaterials have catapulted them to the forefront of research in tumor therapeutics. A variety of nanomaterials, including liposomes, solid lipid nanoparticles (SLNs), polymeric micelles (PMs), dendrimers, mesoporous silica nanoparticles (MSNs), quantum dots (QDs), carbon nanotubes (CNTs), and metallic/magnetic NPs, are proving their potential in transforming cancer treatment.[34] These promising nanomaterials provide targeted drug delivery, improved stability, controlled release, and better penetration into tumor tissues. Additionally, they facilitate multimodal imaging, photothermal therapy, and personalized medicine approaches. Therefore, nanomedicine is an exciting prospect in propelling tumor therapeutics' evolution and addressing the difficulties associated with conventional cancer treatments. The succeeding sections will discuss the specific roles of nanomaterials in different areas of cancer treatment, including surgery, chemotherapy, immunotherapy, radiotherapy, and more, underscoring their significant contributions to enhancing patient outcomes and reshaping cancer care.[35]

2.2.1 Surgery

Unlike conventional surgery, which often includes removing diseased tissues and causing potential damage to surrounding healthy ones, nanomaterials offer a valuable tool for efficient and rapid hemostasis, enhancing safety during surgical procedures. Successfully.[36] A nanocomposite porous gel from carbon nanotubes and chitosan derivatives, demonstrating exceptional hemostatic performance on deep traumatic bleeding. Additionally, microscopic tumors, often difficult to discern by the naked eye, significantly challenge surgical effectiveness. However, with the aid of nanotechnology, tumor margins and adjacent critical structures can be illuminated, sentinel lymph nodes can be mapped, and residual tumor cells and micrometastases can be effectively labeled. This considerably improves detection resolution and provides practical guidance for tumor removal.[36,37]

2.3 Chemotherapy

While traditional chemotherapy is widely utilized, it is not tumor-specific and can damage normal tissue, leading to patient discomfort. It also necessitates repeated administration due to rapid clearance from the body and can result in drug resistance, which reduces patient survival rates. However, NPs can be engineered for specific binding to cancer cells and accumulation at the tumor site, resulting in a highly efficient, low-toxicity therapeutic approach that can overcome tumor drug resistance.[38] Through the exploitation of TME characteristics such as pH, redox gradients, enzyme activity, hypoxia, or specific cell surface receptors, NPs can achieve targeted drug delivery and localized drug release. For instance, lactic acid-modified mesoporous silica NPs have demonstrated specific binding to desialylated glycoprotein receptors on hepatocellular carcinoma cells, thus addressing the drawbacks of non-specific chemotherapeutic drugs.[39] Furthermore, nanocarriers have the potential to deliver multiple therapeutics simultaneously, irrespective of their properties, to maximize treatment efficacy. For instance, Dai et al. reported a self-assembling nano capsule structure for combined drug delivery, while Huang et al. constructed a system for the co-delivery of paclitaxel and vincristine to brain tumors. These integrated strategies, including vincristine's multifaceted mechanisms (e.g., apoptosis induction, anti-angiogenesis, and TME modulation), often enhance therapeutic outcomes.[40]

2.4 Current status and challenges in the translation of cancer-nanomedicine

2.4.1 Current status of cancer-nanomedicine

Nanomedicine formulations have had a significant impact on the global healthcare system and pharmaceutical market. Currently, approximately 100 nanomedicine-based formulations have been approved by regulatory agencies such as the FDA and the European Medicines Agency (EMA). The number of these formulations is increasing annually, with various cancer nanomedicine iterations of previously approved drugs undergoing clinical trials to evaluate their efficacy compared to traditional dosage forms. This growth is driven by increased research and development (R&D) and market demand for innovative drug delivery solutions. The worldwide portfolio of approved cancer nanomedicines sanctioned by the FDA, EMA, Russian Federation Ministry of Public Health (RFMPH), Korean Ministry of Food and Drug Safety (MFDS), and National Medical Products Administration (NMPA)(China) are dominated by five kinds of the nanomedicine: liposomal and lipid nanoparticles, polymeric micelles/conjugates, nanocrystal suspensions, inorganic nanoparticles (e.g., iron oxide, hafnium oxide), and albumin or recombinant protein-based nanocarriers.[41,42]

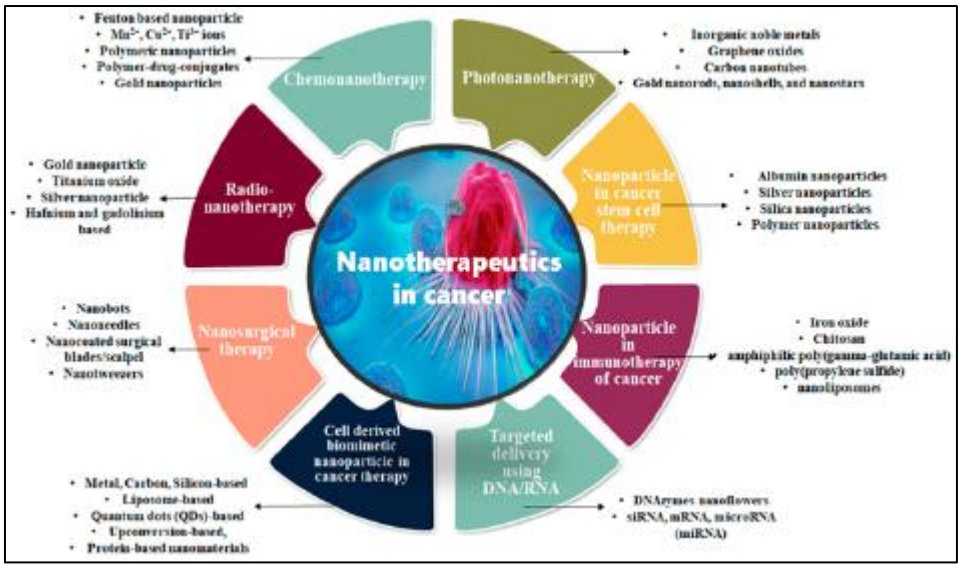


Figure 6: Current management of cancer by nanomedicine

The clinical pipeline continues to expand robustly. As of 2021, alongside the ~100 commercially available nanomedicines, a further 563 candidates were advancing through clinical trials or late-stage development. Over half of these trials (53 %) are Phase I/II studies, and the vast majority target oncology indications. Recent cancer nanomedicines (as catalogued in ClinicalTrials.gov) employing passive/active targeting, or stimuli-responsive strategies, and currently undergoing various stages of clinical trials. Despite this considerable investment and pipeline, the clinical translation of cancer nanomedicine has been marked by several high-profile failures that provide critical lessons for the field. [43]

A prime example is the case of MM-302, a HER2-targeted liposomal DOX. Despite a strong preclinical rationale, a Phase II trial (NCT02213744) in HER2-positive metastatic breast cancer failed to demonstrate a significant improvement in progression-free survival over standard-of-care regimens. This failure has been attributed to several factors, including insufficient proof of superior tumor targeting in vivo and the formidable biological barriers. Similarly, BIND-014, a prostate-specific membrane antigen (PSMA)-targeted docetaxel nanoparticle, showed promising early-phase results but failed in subsequent larger trials for prostate and lung cancers. Post-hoc analyses suggested that patient stratification based on PSMA expression was inadequate, and the anticipated enhancement of the therapeutic index was not fully realized in an unselected patient population. Etirinotecan Pegol (NKTR-102) failed to demonstrate efficacy in a clinical trial for patients with active brain metastases. The failure was attributed to an inability to cross the intact BBB, resulting in no significant drug accumulation in the EPR-negative brain tumors. These examples underscore that nanomedicine failures often stem from biological heterogeneity rather than flawed nanochemistry, therefore necessitating the development of more predictive preclinical models and robust biomarkers for effective patient stratification in clinical trials.[44-46]

3 CONCLUSION

The number of nanotherapeutics in drug development rapidly increases, but clinical success remains modest. This indicates persistent issues that require attention. Although each cancer nanotherapeutic presents distinct concerns, key bottlenecks include scalability, cost, accessibility, biological challenges such as biodistribution, safety, and regulatory hurdles. Emerging nanomedicine strategies have opened new avenues for precision cancer therapy by improving drug delivery, enhancing therapeutic efficacy, and minimizing the adverse effects associated with conventional cancer treatments. Nanotechnology-based drug delivery systems, including liposomes, polymeric nanoparticles, lipid nanoparticles, dendrimers, and inorganic nanocarriers, offer promising approaches for the targeted delivery of anticancer agents to tumor tissues. Furthermore, advances in stimuli-responsive nanocarriers, multifunctional nanoparticles, and nanotechnology-assisted immunotherapy have demonstrated considerable potential for overcoming drug resistance, improving tumor penetration, and modulating the tumor microenvironment. Integration of nanomedicine with precision medicine, biomarker identification, artificial intelligence, and personalized therapeutic approaches may further improve treatment selection and patient outcomes. Despite these advances, challenges related to biocompatibility, toxicity, biodegradability, large-scale manufacturing, regulatory approval, and clinical translation remain significant barriers to widespread clinical application. Future research should focus on developing safer, more selective, reproducible, and cost-effective nanomedicine formulations supported by robust preclinical studies and well-designed clinical trials. Overall, the continued advancement of nanomedicine, combined with personalized treatment

strategies, holds substantial promise for transforming cancer management and achieving more effective, targeted, and patient-specific therapeutic outcomes.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

N*o* conflict of interest to be disclosed.

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