









TAILORED NANOPARTICLES IN PRECISION ANIMAL AND HUMAN ONCOLOGY: ENGINEERING TUMOR-SELECTIVE DELIVERY AND MICROENVIRONMENT INTERPLAY

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ABSTRACT

Precision oncology aims to provide personalized cancer treatment to maximize efficacy while minimizing systemic toxicity. Conventional therapies such as chemotherapy and radiotherapy have the drawbacks of lacking specificity in their toxicity, tumor selectivity, and resistance. Tailored nanoparticles (NPs) have demonstrated outstanding potential to remove such barriers by infiltrating tumors selectively, releasing their cargo in a controlled manner, and by altering the tumor microenvironment (TME). This review summarizes recent advancements in NPs engineering, including lipid-based, polymeric, inorganic, and hybrid carriers, as well as surface conjugations and stimuli-responsive designs that can improve targeting specificity. The complex interactions of NPs with the TME have been outlined, and strategies to address the adverse effects of hypoxia, acidity, enzyme activity, and extracellular barriers are discussed. Applications to targeted chemotherapy, gene and RNA therapeutics, photothermal and photodynamic therapies, immunotherapy, and theranostics are discussed in animals and humans, along with preclinical and clinical translation successes. Challenges and considerations towards successful translation into clinical practice are outlined. Overall, tailored NP-based therapy is highly encouraging for reengineering cancer treatment with precision, efficacy, and versatility in the era of next-generation oncology.

Keywords: Precision Oncology, Nanoparticles, Cancer, Tumor microenvironment, Chemotherapy.

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1. INTRODUCTION

Cancer is recognized as one of the predominant causes of global mortality, and each form displays a unique genetic profile (Li et al. 2020). Precision oncology has evolved to identify the most effective treatment that fits the patient's exact genetic profile and other distinct features that make each patient different. Every patient possesses a distinct genome, epigenome, proteome, microbiome, diet, lifestyle, and other factors that all combine to affect oncogenesis, disease progression, available therapeutic strategy, drug tolerance, regression, and recurrence (Akkız et al. 2025). Cancer is a heterogeneous set of diseases, implying that not only are there differences between cancer cells from different patients, but also between cancer cells from the same patient (Kalla et al. 2025). Cancer is constantly evolving to avoid death, and this is why no single drug has worked to cure cancer. Precision oncology currently involves applying a combination of specific patient features to guide immunotherapy and precision therapies (Bode and Dong 2018).

Recent therapeutic options, including chemotherapy, radiation therapy, immunotherapy or surgery, are usually limited to other issues, which include toxic side effects, inaccuracy and inability to destroy tumors. Traditional cancer treatments tend to be inaccurate and ineffective as well as develop resistance to treatment and cancer recurrence (Afkhami et al. 2024). However, all treatment methods have limitations that require additional intervention or are not precise in their targeting, leading to additional negative impacts on the person. An example is radiation and chemotherapy therapy; the treatment is not specific to attacking cancer cells and thus it destroys both normal and cancerous cells, leading to undesirable side effects. Furthermore, such interventions cannot fully eliminate tumor and metastasis (Yarahmadi and Afkhami 2024). To be effective, cancer patients require new and innovative therapies that could minimize side effects and optimize efficiency. Over the last few decades, several advances in these and other fields in medical research have opened new possibilities in combating cancer with refined targeting with enhanced

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therapeutic potential. Nanoparticle (NP) technology, especially in the production of numerous pharmaceuticals, has made substantial progress today (Parupudi et al. 2022). The employment of promises to enhance the effectiveness of treatments and diagnostics of a broad array of diseases, including cancer (Khan and Hossain 2022). NPs are non-toxic, stable, and biocompatible, making them an effective means of drug delivery (Sharma et al. 2021).

NPs have become a paradigm shift in the diagnostic and treatment of animal oncology, as they provide a more targeted approach, reduced toxicity, and greater therapeutic efficacy (Sv et al. 2024; Puttasiddaiah et al. 2025). Their capacity to deliver drugs directly to tumor tissues has shown promise in controlling complex cancers in veterinary patients. Indicatively, the application of NP-mediated thermal therapy has been found to induce notable levels of immunomodulatory effects in canine tumors which has enhanced the rate of therapeutic response (Castelló et al., 2022; Ahmed et al. 2022). Nanocarrier systems have also demonstrated the potential to enhance traditional osteosarcoma therapy by increasing drug penetration and slowing drug release (Sapino et al., 2022; Xu et al., 2025). Nanotechnology-based photodynamic therapy has been seen to be effective in the management of oncological cases in dogs and cats (Guimarães et al., 2022). Moreover, cold atmospheric plasma combined with nanoparticles has become an innovative therapeutic modality with synergistic anticancer effects (Wang et al., 2025). Companion animals have naturally occurring cancers that have significant biological and molecular similarities with human malignancies and are therefore useful translational models of tumor behavior, progression, and therapeutic responses (Oh and Cho, 2023).

The progression and metastasis of cancer are regulated by the intricate interactions between immune cells and cancer cells within the tumor microenvironment (TME) (Buhrmann et al. 2014). TME is important in controlling cancer cell survival, proliferation and metastatic process. Its interactions between cellular and structural constituents promote tumor aggression and allow dissemination to distant organs. There is growing evidence of the role of both innate (e.g., macrophages, neutrophils, dendritic cells, NK cells) and adaptive (e.g., T and B cells) immune cells in influencing the behavior of tumors and bolstering resistance to treatment (Hinshaw and Shevde 2019). In addition to causing therapy resistance, these complex interactions also restrict drug delivery, which points to the necessity of developing NPs-based modalities capable of sensing or penetrating the TME to improve precision oncology treatment efficacy (Hristova-Panusheva et al. 2024). This review will emphasize recent developments in tumor-specific targeting in NPs engineering and tumor microenvironment modulation and provide insights into the significant role of precision oncology.

2. TUMOR-SELECTIVE ENGINEERING

2.1. Principles of Tumor Selectivity

As the study on cancer and nanomedicine has progressed, research has begun to focus on the effective and accurate administration of nanomedicine to the tumor sites. The purpose of this intervention is to reduce the systematic toxicity, focusing on tumor tissue, the TME, specific cells, and organelles and enhancing therapeutic potential (Teng et al. 2025). Tumor targeting has been considered an appealing approach to enable access to tumors and to prevent penetration into the normal tissue interstitium. There are two categories of tumor targeting: passive and active; active targeting is triggered when uncontrolled deposition within tumors occurs (Xu et al. 2020). The targeting of active and passive NPs is shown in Fig. 1.

Passive targeting constitutes the movement of nanocarriers into the interstitium and cells by convection or passive diffusion across leaky tumor capillary fenestrations (Attia et al. 2019). The EPR effect is responsible for the selective accumulation of nanocarriers and drugs. The EPR effect is currently emerging as the gold standard for designing cancer-targeting drugs. EPR effect is a guiding principle used in all nanocarriers. Additionally, the EPR effect can be applied to nearly all rapidly growing solid tumors (Subhan et al. 2021). In fact, EPR effect is evident in nearly every malignant tumor of humans except hypovascular tumors like prostate cancer or pancreatic cancer (Sharifi et al. 2022).

However, there are some limitations to accessing the tumor passively. (i) The passive targeting is based on tumor vascularization and angiogenesis (Attia et al. 2019). Therefore, the vascular permeation of nanocarriers will depend on the tumor and anatomical locations. (ii) As stated earlier, the elevated interstitial fluid pressure of solid tumors prevents the effective absorption and homogeneous distribution of drugs within the tumor (Böckelmann and Schumacher 2019). The correlation between size and the EPR effect is due to elevated interstitial fluid pressure within tumors, in which larger, longer-circulating nanocarriers (100 nm) tend to remain longer in the tumor. In contrast, smaller molecules are readily diffused (Sharifi et al. 2022).

Active targeting, also termed ligand-mediated targeting, is the process where affinity ligands are bound to the surface of NPs to provide some deposition and internalization by the targeted disease cells. In that regard, ligands are selected to attach to surface molecules or receptors that are upregulated in disease-related tissues or organs, cells or intracellular region (Bandyopadhyay et al. 2023). Active-targeted material must be in proximity to their target to take advantage of this enhanced affinity (Didamson et al. 2022). Thus, the strategy is directed at enhancing the number of interactions between NPs and cells, as well as cellular drug uptake, without significantly altering systemic

biodistribution (Zhang et al. 2023). Physicochemical characteristics such as the density of the ligand, the size of the NPs or the selection of the targeting ligand may also potentially influence the effectiveness of the approach employed, evaluated in vitro and with relevance in vivo (Yoo et al. 2019).

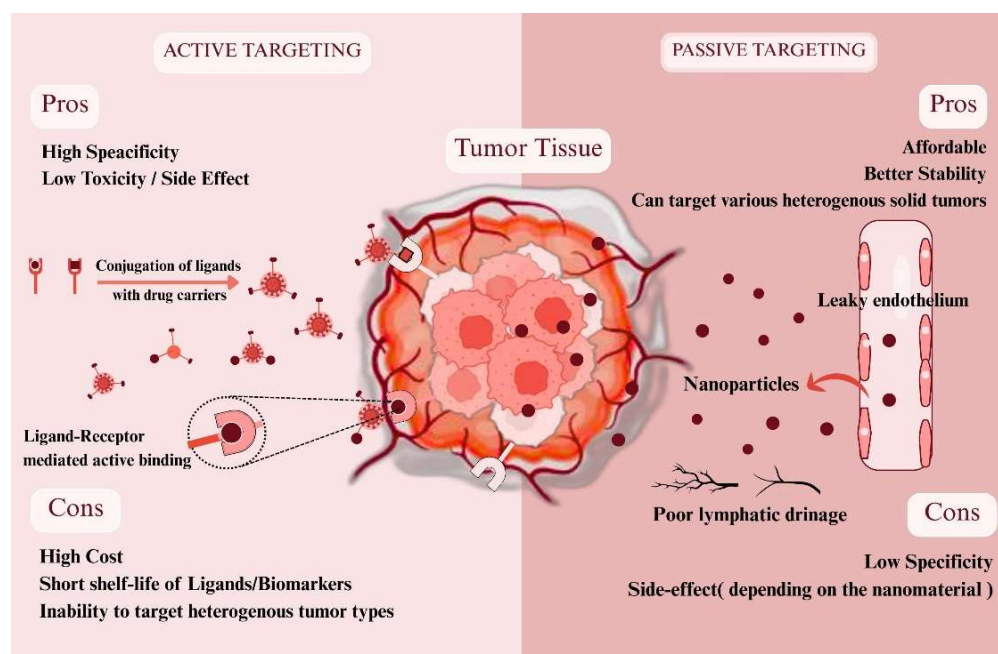


Fig. 1: A diagrammatic illustration of the targeting of active and passive NPs in tumors that contrasts the EPR effect with ligand-receptor mediated binding.

The primary active targeting mechanism is the identification of the ligand by the target substrate. Representative ligands include antibodies, peptides, proteins, sugars, nucleic acids, and small molecules such as vitamins (Attwood et al. 2020). Proteins, sugars, or lipids carried on the surface of cells or diseased organs can be the target molecules. The multivalent nature of the NP amplifies the interaction between ligand-modified NPs and the corresponding antigen: the more copies of the ligand, the higher cumulative affinity of the NP towards its target (Vaughan et al. 2020). In the active targeting strategy, two cellular targets can be distinguished: (i) the targeting of cancer cells and (ii) the targeting of tumoral endothelium. In the future, actively targeted NPs are also seen as a potential synergistic approach to EPR to advance the efficiency of cancer nanomedicines (Shi et al. 2020).

2.2. NPs Platforms and Surface Functionalization for Tailored Design

Delivery platforms include liposomes, targeted polymer drug conjugates, polymeric micelles and dendrites (Jain and Chauhan 2019). They are all made up of collections of macromolecules on which drugs are conjugated, dissolved, or trapped. The clinical approval of numerous liposomal drug delivery systems, such as those for doxorubicin and daunorubicin, has been obtained. The FDA also endorsed Abraxane, an albumin-bound NPs that constitutes paclitaxel, to treat breast cancer (Yuan et al. 2020). The controlled release of drugs at the tumor site can significantly enhance targeting. This may be induced by alterations in the microenvironment or external stimuli at the tumor location (Mi, 2020).

The surface functionalization of liposomes is often performed using aptamers, peptides, antibodies, and small-molecule ligands, based on their use in anticancer treatment (Riaz et al. 2018). Immunoliposomes can be prepared by conjugating antibodies or antibody fragments to the liposome surface using a variety of surface engineering methods. Covalent conjugation of an antibody or its fragment to liposomal lipid is one method of surface functionalization of liposomes. In the alternative method, the antibody is chemically functionalized to make it more hydrophobic by introducing an appropriate substituent, thereby increasing its affinity for liposome bilayers (Rathnaweera et al. 2025). The most recent trend involves the use of antibody fragments (i.e., fragment antigen-binding (Fab⁺)/single-chain fragment variable (scFv)) rather than the entire antibody. Adopting this approach has the primary benefit of preventing the possibility of antibody disintegration in the process of surface engineering aimed at producing immunoliposomes" (Guyon et al. 2020). Fig. 2 demonstrates liposome-based NPs engineering for targeted cancer therapy.

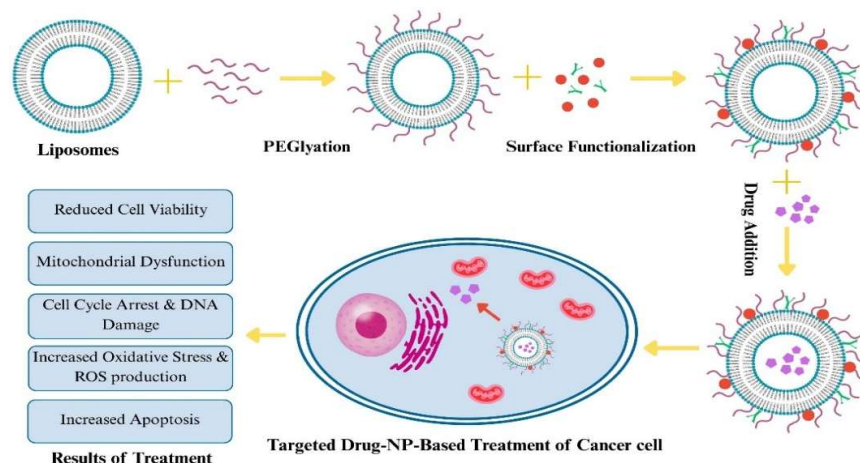


Fig. 2: Diagrammatic depiction of liposome-based NPs engineering for targeted cancer therapy, showing PEGylation, surface functionalization, drug loading, and therapeutic outcomes including ROS generation, DNA damage, mitochondrial dysfunction, and apoptosis.

The polymerization of amino acids forms peptide via peptide bonds that are surface-engineered onto liposomes primarily by covalent and non-covalent bonding (Yuan et al. 2025). Several covalent bonds, including MAL linkage bonds, sulfanyl bonds, peptide bonds, disulfide bonds, and phosphatidylethanolamine-linked bonds, can covalently conjugate peptides to liposomes (Koren and Torchilin 2018). Currently, thioester and disulfide connections have been extensively documented in the literature. Amphipathic peptides and liposomes have been linked by a non-covalent bond (Eroğlu and İbrahim 2020). There are two types of peptides used to functionalize the surface of nanocarriers, such as liposomes, cell-targeting peptide (CTP), and cell-penetrating peptide (CPP). These peptides have receptor-specific internalization and non-specific binding, respectively (Riaz et al. 2018).

Folate, carbohydrates, affibodies, and other small molecules have been used as targeted ligands to modify liposome surfaces and combat cancer (Khan et al. 2020). Folate-targeted liposomes incorporating imatinib, a suppressor of the platelet-derived growth factor receptor, have been developed for cervical cancer therapy. Although liposomes have the potential in cancer treatment, they are facing several challenges such as stability, storage, poor oral bioavailability, leakage of drug molecules and immune recognition (Riaz et al. 2018). Targeting is dependent on key design elements including size, charge, shape, PEGylation, and ligand density. The costs of production and scalability are also significant impediments that need additional research and development (Hussain et al. 2019).

2.3. Stimuli-Responsive NPs

Nanoparticulate systems that are receptive to signals can deliver therapeutic drug molecules, without influencing the area surrounding the tumor site (Mi, 2020; Ghafoor et al., 2024). The stimuli responsive systems of NPs are classified as 2 types: internal (pH, ROS, hypoxia, enzyme, redox) and external (radiation, electromagnetic, thermal) stimuli according to the mode of induction of the delivery of the drug (Thomas et al. 2020) (Fig. 3). The discharge of the drug of the NPs in pH-dependent activity may be regarded as the most effective method relative to alternative drug release approaches. Tumor microenvironment is acidic due to the lactic acid accumulation associated with tumor growth (Bahrami and Tafrihi 2023). The pH-sensitive NPs in this acidic medium activate stimuli-responsive behavior, thus altering the molecular composition of the material and initiating the drug liberation (Wells et al. 2019).

Different enzyme expressions can be caused by an ailment, and this may result in an increase of the levels of hyaluronidase, cathepsin, trypsin, proteinase K, thrombin, etc (Jamal et al. 2025). The enzymes that are upregulated can be used to modulate drug release in nanocarriers, disintegration of polymer frameworks, physical destruction of nanocarriers and disruption of interaction involving the drug and the transport agent in the TME (Mi, 2020). Enzymes have the potential to destabilize NPs using the biological recognition and enzymatic activity. Enzymes are divided into major classifications: hydrolase and oxidoreductase. Hydrolase enzymes can break a chemical bond by adding water molecules; oxidoreductase enzymes can catalyze an oxidation/reduction reaction, and the NPs are destroyed (Rabiee et al., 2019).

ROS accumulation and propagation were reported to be higher in cancer cells than normal cells because the process of various oncogene stimulation, inflammation, coupled with mitochondrial dysfunction, is stimulated (Zhao et al. 2023). In the presence of various hydroxyl radicals ($\bullet\text{OH}$), superoxide anions (O^{2-}), peroxynitrites (ONOO^-) and hydrogen peroxides (H_2O_2), the use of ROS-cleavable bonds in cargos for efficient and prolonged drug release is a developing area of study interest (Vasvani et al. 2024). The release of drugs through NPs is determined by the chemical structure and reaction mechanism of the linkers. Key parameters in drug delivery mechanisms include ROS-mediated disintegration of the carrier system (Tao and He 2018).

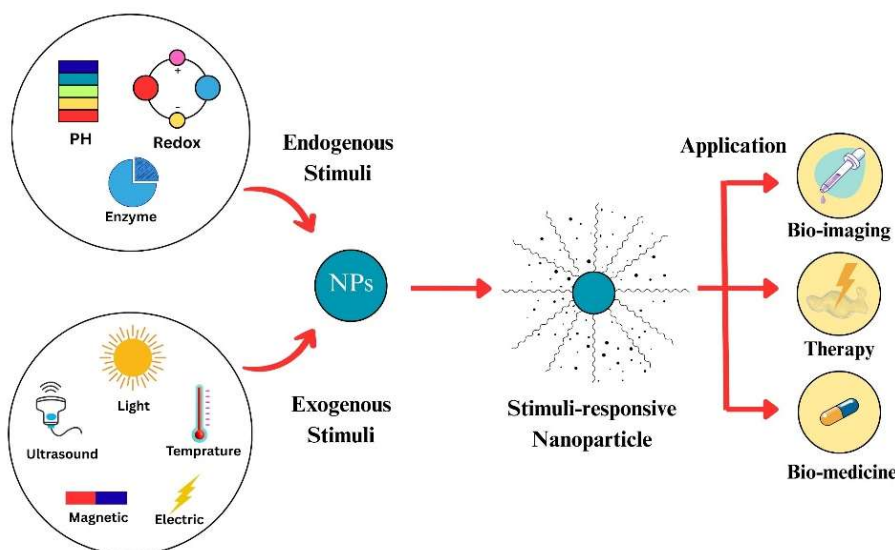


Fig. 3: Overview of stimuli-responsive NPs activated by endogenous or exogenous signals.

When combined with external stimuli, e.g., light, temperature, or mechanical stimuli, internal stimuli may lead to increased drug release (Wells et al. 2019). The TME itself can often supply one type of stimulus to enable drug release, although this method may not be effective in the drug release of some types of NPs. Thus, external stimuli may offer a supplementary drive to achieve the highest drug bioavailability potential. A drawback of externally triggered materials, however, is that they cannot reach the location of the tumor to cause the relevant release of the drug (Pham et al. 2020).

3. TUMOR MICROENVIRONMENT (TME) INTERPLAY

3.1. Composition and Dynamics of the TME

The TME is a dynamic ecosystem of tumor that is supported and modified by tumor cells in their evolution process (De Visser and Joyce 2023). Besides the tumor cells, the typical structure of the TME also consists of stromal cells (adipocytes, fibroblasts, endothelial cells, and stellate cells), immune cells (B cells, T cells, natural killer cells, neutrophils, macrophages and dendritic cells), extracellular matrix and blood vessels (Anderson and Simon 2020). The TME protects and harbors the tumor cells in a variety of forms once formed, including altering angiogenesis to help tumors grow; triggering stromal cells to create a physical barrier to impeding tumor infiltration by lymphocytes (Mhaidly and Mechta-Grigoriou 2021); modulating metabolisms to undermine T-cell activity (Zhang et al. 2020); and recruiting immunosuppressive cells to the TME (Groth et al. 2019).

3.2. TME as a Barrier and Target

Cancer cells can only generate heterogeneity and increase multi drug resistance in tumor cells through dynamic interaction with these cellular and acellular entities of TME (Baghban et al. 2020). Furthermore, there are numerous and diverse specialized microenvironments within TME. Hypoxia occurs in a tumor because of unregulated growth and a lack of sufficient vascularization, generating oxygen-deficient zones within TME (Ciepla and Smolarczyk 2024). Hypoxia-inducible factor-1 (HIF-1) is predominantly involved in the regulation of this condition by activating angiogenic signaling, oncogenic cell endurance, and epithelial-mesenchymal transition (EMT) (Zhang et al. 2021). Nevertheless, it has also opened avenues of intervention, and some of the approaches being explored include HIF-1 inhibitors, metabolic regulators, i.e. metformin, and hypoxia prodrugs that are at the clinical trial stage (Curry et al. 2018).

Cancer cell metabolism is highly dependent on glycolysis, which is enhanced by hypoxia and vascular insufficiency resulting in lactate accumulation and extracellular acidification (Chelakkot et al. 2023). Although early acidity can trigger cancer cell death, chronic low pH induces tumor aggressiveness and therapy resistance (Abou Khouzam et al. 2022). Acidic microenvironment also inhibits antitumor by suppressing effector T lymphocytes and stimulating pro-tumor immune cultures (Boussadia et al. 2020). These aspects render acidity a therapeutic barrier and target, and advances are being pursued in small molecule-based inhibitors and pH-dependent drug delivery systems (Zhong et al. 2020).

Inflammation has both tumor suppressing and promoting effects in cancer development (Jang et al. 2021). The acute inflammation creates an antitumor environment by discharge of cytokines, chemokines, and cytotoxic factors

that limit tumor expansion. But chronic inflammation fosters immunosuppressive TME through macrophages M2 and myeloid-derived suppressor cells (MDSCs) as well as regulatory T/B cells that promote proliferation, metastasis and therapeutic resistance (Zheng et al. 2021). This pro-tumor inflammatory state is mediated by several signaling cascades such as JAK-STAT, NF- κ B, MAPK and TLR. Inhibition of inflammation with NSAIDs (aspirin, sulindac, COX-2inhibitors) statins, IL-6, and natural products (e.g. curcumin, resveratrol) are under clinical or preclinical development (Nisar et al. 2023).

3.3. NPs–TME Interactions

Enhancing penetration and retention (EPR) requires an insight into the associations between NPs and TME. The effectiveness of NPs is increased by TME-modulating techniques such regulating blood vessels or focusing on tumor-associated macrophages (Kumari and Tamrakar 2024). As immune modulators, NPs can improve anti-tumor immunity or lessen negative immune-related consequences (Antônio et al. 2018). By directly delivering immunostimulatory chemicals (such as cytokines) to antigen-presenting cells, they can enhance tumor infiltration and T-cell activation (Korangath et al. 2020).

The EPR effect is the tendency of NPs and macromolecules to selectively aggregate in solid tumors due to the leakiness of the tumor vasculature and poor lymph circulation, resulting in greater tumor enhancement (Thomas and Weber 2019). It has been found that the EPR effect differs considerably among tumor types, being strong in tumors like hepatocellular carcinoma but weak in poorly vascularized tumors such as pancreatic and prostate cancers, owing to differences in the density of vasculature, interstitial fluid pressure, and stromal composition. Administration of a very large proportion of the NPs (usually \sim 0.7%) will typically reach the tumor, restricting the therapeutic effect (Subhan et al. 2023). Most evidence of EPR comes from animal studies and xenograft models, which exaggerate EPR in human tumors (Lee et al. 2018; Miao et al. 2020; Paus et al. 2021; Pan et al. 2022). As a result, it is crucial to integrate the EPR effect with other strategies, such as active targeting, targeting tumor microenvironment, or personalized imaging to facilitate more efficient delivery of nanomedicine (Prabhakar et al. 2013).

To address such barriers, a diversity of strategic alterations has been devised to enhance NPs delivery. PEGylation is the most used strategy because it extends the systemic circulation and decreases clearance mediated by mononuclear phagocyte system (Grundler et al. 2023). Similarly, NPs size and surface charge optimization improves penetration across the extracellular matrix (ECM); NPs in disk shape or with negative surface show increased ability to diffuse to high-density and tumor stroma (Cassani et al. 2025). The enzymatic ECM modulation is another possible method where an enzyme like collagenase or hyaluronidase can destroy structural barriers and lower the density of the ECM, which will enable the penetration of the NPs deeper, and enhance clinical access to the tumor core (Yu et al. 2024). All these methods contribute greatly to the penetration and retention of NPs in solid tumors and are commonly used in conjunction with the EPR effect to achieve optimal therapeutic effects (Sharifi et al. 2022).

4. APPLICATIONS IN PRECISION ONCOLOGY

The development of smart nanomaterials can be used to track drug liberation or biomarkers generated during monitor tumor response and provide real-time assessment of therapeutic efficacy. This allows doctors to make timely adjustments to treatment plans, thereby increasing treatment efficacy and the precision of medicine (Ju and Cho, 2023). All things considered, the use of NPs in tailored cancer treatment significantly enhances the capabilities of conventional therapies, resulting in more accurate, efficient and customized care. The major applications of NPs in precision oncology, along with their therapeutic approaches, advantages, and supporting literature, are outlined in Table 1.

Table 1: Overview of Application Areas, Approaches, Examples, and Advantages

| Application Area | Approach | Examples & Advantages | Representative References |
|-----------------------------|---|--|---------------------------|
| Targeted Chemotherapy | MSNs, ligand-functionalized NPs, responsive delivery systems | High tumor specificity, multidrug co-delivery, reduced toxicity | Mann et al. 2024 |
| Gene & RNA Therapeutics | Lipid NPs (LNPs), polymeric carriers, exosome-mimetic vesicles for siRNA/mRNA/CRISPR | Protection from degradation, precise gene modulation | Godbout and Tremblay 2022 |
| Photothermal / Photodynamic | Gold nanorods, polydopamine, and oxygen-generating MOF-based nanocarriers for NIR/PDT therapy | Improved tumor ablation, hypoxia mitigation, and enhanced ROS production | Zuo et al. 2024 |
| Immunotherapy | Nanodelivery of checkpoint inhibitors, STING agonists; macrophage reprogramming (M2 \rightarrow M1) | Localized immune activation, enhanced T-cell responses | Huang and Zhang 2024 |
| Integration | & Imaging-functionalized NPs (MRI, CT, PET) | Real-time tracking, personalized and adaptive therapy | Siddique and Chow 2022. |
| Theranostics & Monitoring | | | |

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5. PRECLINICAL AND CLINICAL ADVANCES

Numerous NPs-based formulations have already entered clinical practice and allow gaining insight into the opportunities and challenges of nanotechnology application in precision oncology.

5.1 Approved Nanomedicines and Their Clinical Performance

Several therapeutics based on NPs have also been approved to be used in clinical practice. Patients have been introduced to liposomal doxorubicin (Doxil(R)), albumin-bound paclitaxel (Abraxane(R)) and a type of imaging (iron oxide particles) (Aljabali and Obeid 2020). These achievements validate the idea of nanomedicine yet also demonstrate how challenging it can be to commercialize new platforms into the clinic. The reason is that clinical trials at times reveal discrepancies between the early encouraging preclinical outcomes and the disappointing clinical performance. The issues include stability of NPs in human plasma, inter-patient variability and scale-up of manufacturing (Chen et al. 2022).

5.2. Personalized Nanomedicine and Biomarker-Guided Therapies

NPs design refinements and patient stratification and combination strategies will facilitate clinical success. Oncology is the future of personalization. Nanomedicines can contain biomarkers that can report on drug release or tumor response, and it may permit dynamic treatments to be undertaken (Caracciolo et al. 2019). Artificial intelligence/ big data analytics can potentially be used to identify the sub-group of patients that would be most likely to react to a particular nanomedicine (Chattu 2021).

6. CHALLENGES IN NANOMEDICINE TRANSLATION

6.1. Scale-Up, Manufacturing, and Quality Controls

It is not a straightforward task to produce NPs on a large scale with good consistency in quality. Minor changes in raw materials or processing conditions may influence the particle size, stability and the ability to encapsulate (Manno et al. 2025). Clinical translation requires Good Manufacturing Practice (GMP) procedures and robust quality control (Lungu et al. 2019).

6.2 Stability, Shelf-Life, and Storage Requirements

Nanocarriers have several storage requirements to remain stable. The widespread clinical adoption requires long shelf-life and easy handling procedures (Kardani 2024).

6.3 Economic and Ethical Considerations

The development of nanomedicine is capital intensive. The challenge of providing innovation and affordability and fair access to such advanced therapies is ethical and economical (Mangeolle et al. 2019). All these barriers can be overcome with the help of international collaborations and state support (Omidifar et al. 2021).

7. FUTURE DIRECTIONS AND EMERGING TRENDS

7.1 Next-Generation Materials and Smart Nanocarriers

Advanced functionalities are being integrated into emerging nanomaterials, including shape-shifting carriers, multi-stimuli responsiveness, self-assembling nanocomposites. The purposes of these advanced systems are to enhance tumor penetration, diminish clearance, and respond to dynamic tumor conditions (Rahimnejad et al. 2024).

7.2 Artificial Intelligence and Machine Learning in Nanomedicine

AI-based design tools can be used to predict properties of NPs, optimize formulations, and even create custom treatment regimens using omics data of patients. Machine-learning models, which examine big datasets of imaging and clinical trials, can accelerate the development of novel nanomedicines (Dirisala et al. 2020).

7.3 Theranostics and Integrated Treatment Platforms

Theranostics NPs that aim at incorporating therapy and diagnostics within the same system, offer real-time assessment of drug delivery and tumor reaction. This integration will give the clinicians the opportunity to make timely amendments in the treatment plans which will improve patient outcomes (Anani et al. 2021).

7.4 Regulatory Harmonization and Global Collaboration

The complexity of nanomedicines requires cooperation between scientists, doctors, players in the industry, and regulators across the world. International organizations that harmonize structures, share data and integrate testing

protocols can hasten the safe and effective development of nanotherapeutics (Miernicki et al. 2019).

8. CONCLUSION

Tumor-selective NPs have been designed as a novel therapeutic tool in precision oncology, delivering therapeutic index, enhancing efficacy, and combining with the tumor microenvironment. Engineering innovation, particularly the functionalization of surfaces and the development of stimuli-responsive systems, has tremendous potential to overcome barriers to conventional cancer therapies. Although these constitute promising clinical results, specific challenges remain, including scaling difficulties, patient heterogeneity, and regulatory translation. The NPs technology has been defined with extreme caution, and regarding the novel biomarker-driven therapies and artificial intelligence, the power of tailored NPs has the potential to revolutionize the field of oncology and bring the vision of personalized medicine into reality soon.

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