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Next-Generation Nano medicine in Oncology: Multi-Cancer Insights into AI-Guided Precision Therapies

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Abstract:

Background: Cancer therapy continues to face major challenges due to systemic toxicity, therapeutic resistance, and tumor heterogeneity, underscoring the need for innovative treatment paradigms. **Objective:** This review examines advances between 2019 and 2024 in artificial intelligence (AI)–integrated nanomedicine for multi-cancer applications, with a focus on liver, breast, renal, and brain tumors. **Methods:** A comprehensive analysis of recent literature was performed, covering nanocarrier innovations, AI-driven biomarker discovery, omics-based integration, and outcomes from preclinical and clinical studies. **Results:** Smart nanocarriers demonstrated significant promise across tumor types: ASGPR- and GPC3-targeted formulations in hepatocellular carcinoma, subtype-specific nanotherapies in breast cancer, VEGF- and tyrosine kinase inhibitor–loaded nanoparticles in renal cell carcinoma, and blood–brain barrier–penetrating systems for glioblastoma. AI models played a pivotal role in enhancing patient stratification, predicting therapeutic responses, and guiding the rational design of nanocarriers with improved pharmacokinetics and tumor penetration.**Conclusion:** AI-guided nanomedicine is emerging as a disruptive frontier in oncology, offering precision, personalization, and enhanced translational potential across diverse tumor landscapes.

Keywords: cancer nanomedicine; precision oncology; multi-omics; artificial intelligence; hepatocellular carcinoma; breast cancer; renal cell carcinoma; glioblastoma.

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1. Introduction

Cancer continues to rank among the most formidable global health burdens, with mortality rates remaining high despite decades of research into early detection, novel drug development, and

therapeutic refinements. Conventional cancer therapies chemotherapy, radiotherapy, and targeted biologics are often hindered by systemic toxicity, drug resistance, and inter-patient heterogeneity. In this landscape, nanomedicine has emerged as a transformative platform capable of enhancing drug solubility, tumor targeting, and controlled release, while simultaneously enabling diagnostic monitoring through theranostic design [1-2].

What distinguishes *next-generation nanomedicine* from earlier platforms is its integration with artificial intelligence (AI) and multi-omics data streams. By harnessing genomic, proteomic, metabolomic, and immunomic insights, AI models are increasingly able to stratify patients, predict therapeutic response, and guide the rational design of nanocarriers tailored for specific tumor phenotypes [3]. The convergence of nanotechnology, AI, and precision oncology has accelerated translation from bench to bedside, particularly in liver cancer, breast cancer, renal cell carcinoma, and neuro-oncology. This review synthesizes advances from 2019 to 2024, highlighting how AI-guided nanomedicine platforms are reshaping the cancer therapy paradigm [4]. **(Figure 1)**

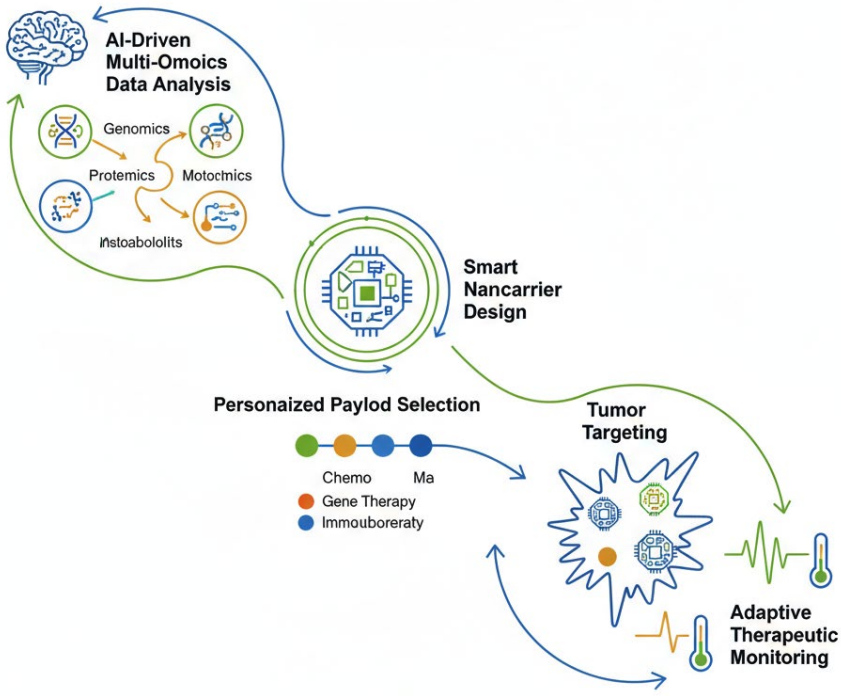

Figure 1: A conceptual schematic of *AI + nanomedicine integration in oncology*.

2. Nanomedicine and AI: A Converging Frontier

Nanomedicine has evolved far beyond its early role as simple drug carriers such as liposomes, micelles, and polymeric nanoparticles, progressing toward the development of smart, stimuli-responsive, and bioengineered nanocarriers capable of responding to tumor microenvironment (TME) cues like pH variations, hypoxia, or enzyme activity [5]. The integration of artificial intelligence (AI) techniques including deep learning, reinforcement learning, and predictive modeling has further expanded the potential of this field by enabling the prediction of patient-specific drug responses, optimizing nanoparticle design for improved biodistribution and tumor penetration, and unifying imaging, pharmacokinetic, and multi-omics datasets into actionable therapeutic strategies [6]. This convergence of nanomedicine and AI is thus fostering the rise of highly personalized platforms that transcend the limitations of one-size-fits-all oncology and pave the way for precision cancer therapeutics [7]. (Figure 2)

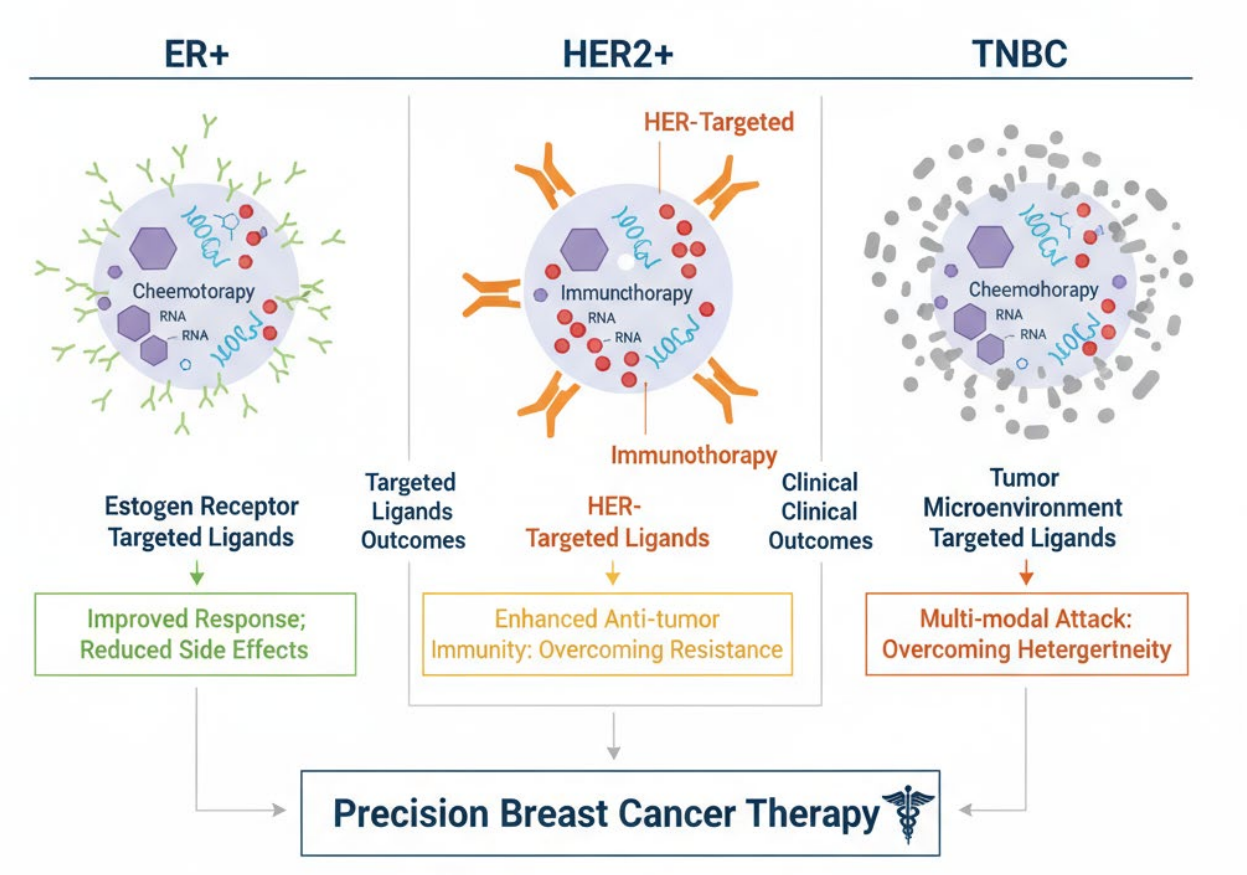

Figure 2: Subtype-specific strategies (ER+, HER2+, and TNBC) in a comparative diagram.

3. Liver Cancer (Hepatocellular Carcinoma, HCC)

Hepatocellular carcinoma (HCC) is the most prevalent form of primary liver cancer and remains one of the leading causes of cancer-related deaths worldwide. Its incidence has steadily increased over the past decade, fueled by risk factors such as chronic hepatitis B and C viral infections, alcohol abuse, and non-alcoholic fatty liver disease [8]. Despite advancements in systemic therapies, including tyrosine kinase inhibitors and immune checkpoint inhibitors, survival outcomes remain poor because most cases are diagnosed at advanced stages, with recurrence and therapeutic resistance presenting major clinical hurdles. Conventional drug delivery approaches are often hindered by the complex architecture of the liver, including its dense stromal environment and dual blood supply, which restrict therapeutic accumulation within tumors while exposing healthy hepatocytes to systemic toxicity [9]. These limitations have spurred the emergence of nanomedicine as a promising approach, offering selective tumor targeting, improved stability of fragile payloads, and reduced off-target side effects.One of the most widely investigated approaches for HCC involves the use of nanocarriers that exploit specific molecular signatures on tumor cells. For example, nanoparticles conjugated with ligands for asialoglycoprotein receptors (ASGPR) or glypican-3 (GPC3), both of which are highly expressed in HCC, have demonstrated enhanced binding and internalization in preclinical models. Similarly, intra-arterial delivery of nanoparticles during transarterial chemoembolization (TACE) has been explored to increase local drug concentrations while minimizing systemic exposure [10]. In addition, stimuli-responsive nanoparticles are being developed to release drugs specifically in response to the tumor microenvironment. Acid-sensitive carriers release payloads in the slightly acidic milieu of HCC, while redox-responsive systems take advantage of elevated glutathione levels within cancer cells. These strategies enable more precise drug release, reducing collateral damage to surrounding tissues and enhancing therapeutic efficacy.Another exciting frontier lies in RNA- and gene-editing therapeutics. Nanoparticle-mediated delivery of small interfering RNA (siRNA) and microRNA (miRNA) has shown great promise in silencing oncogenes and reactivating tumor suppressor pathways [11]. Advances in lipid nanoparticle formulations, many inspired by mRNA vaccine technology, have facilitated efficient hepatic delivery of such payloads. Furthermore, gene-editing platforms such as CRISPR/Cas9 are now being packaged within nanocarriers to target key driver genes implicated in HCC progression, including TERT, TP53, and CTNNB1. These interventions not only offer therapeutic avenues previously inaccessible but also highlight how nanomedicine intersects with the broader field of precision oncology.Artificial intelligence is increasingly being integrated into the design and deployment of nanotherapeutics for HCC [12]. Radiomics and deep learning applied to MRI and CT imaging are being used to predict tumor aggressiveness, therapeutic response, and likely sites of recurrence, thereby refining patient selection for

nanomedicine-based trials. AI-driven analysis of multi-omics datasets, including genomic mutations, proteomic biomarkers such as alpha-fetoprotein, and transcriptomic signatures, allows the identification of patient subgroups most likely to benefit from specific nanoparticle formulations [13]. In parallel, predictive models are being developed to simulate nanoparticle biodistribution and therapeutic efficacy in silico before proceeding to in vivo validation, greatly accelerating the translation pipeline.Several nanomedicine platforms for HCC have already begun to transition from preclinical research to early clinical evaluation. Liposomal formulations of doxorubicin, when incorporated into TACE protocols, have shown encouraging outcomes in early-phase studies [14]. Exosome-derived nanocarriers are being investigated as dual-purpose systems capable of modulating the immune microenvironment while simultaneously delivering gene-silencing payloads. Nevertheless, significant challenges remain. The heterogeneity of the HCC tumor microenvironment makes it difficult to achieve uniform drug distribution, while concerns about nanoparticle accumulation in non-tumor hepatic tissue raise questions of long-term safety. Furthermore, regulatory frameworks for gene-editing nanoparticles are still evolving, complicating their clinical adoption [15].

Taken together, the integration of nanotechnology, omics-driven patient stratification, and artificial intelligence represents a transformative step forward in the management of hepatocellular carcinoma. Although obstacles remain, particularly with respect to consistency, scalability, and safety, the convergence of these technologies offers a roadmap for precision nanomedicine approaches that may redefine outcomes for patients with liver cancer [16].

4. Breast Cancer

Breast cancer remains the most commonly diagnosed malignancy among women worldwide, with subtypes such as estrogen receptor–positive (ER+), HER2-positive (HER2+), and triple-negative breast cancer (TNBC) demonstrating distinct molecular profiles, therapeutic vulnerabilities, and clinical outcomes [17]. Nanomedicine has emerged as a versatile tool to address the heterogeneity of these subtypes, enabling tailored interventions that integrate chemotherapy, targeted agents, and immunotherapy within engineered carriers. From 2019 to 2024, several advances in nanotherapeutic platforms have sought to optimize delivery, reduce systemic toxicity, and overcome resistance mechanisms that limit the efficacy of conventional regimens.For ER+ tumors, where endocrine therapy remains a cornerstone of treatment, nanotechnology has enabled the encapsulation of hormone-blocking agents such as tamoxifen and fulvestrant into polymeric or lipid-based carriers [18]. These nanoformulations enhance bioavailability and improve tumor accumulation, while co-loading synergistic payloads such as CDK4/6 inhibitors offers the possibility of delaying or preventing resistance. The controlled release kinetics of such nanocarriers further ensure sustained receptor blockade, minimizing the fluctuations in plasma

drug levels that often drive suboptimal responses [19].ER2+ breast cancer, which historically benefited from monoclonal antibody therapies such as trastuzumab, has also witnessed a technological shift through the integration of nanomedicine. Antibody–drug conjugates (ADCs) have been enhanced with nanoparticle hybrids that permit higher drug loading, greater tumor penetration, and reduced systemic clearance [20]. Artificial intelligence has played a central role in optimizing these platforms by modeling drug–antibody ratios, predicting nanoparticle–HER2 receptor interactions, and refining payload selection. AI-driven simulation studies have also accelerated the identification of patients most likely to benefit, by integrating genomic HER2 amplification profiles with proteomic signatures, thus enabling biomarker-guided personalization of nano-enabled HER2 therapy [21].

The most transformative progress, however, has been observed in triple-negative breast cancer (TNBC), which lacks targeted receptor expression and is traditionally associated with poor prognosis. Here, nanomedicine has converged with immunotherapy to create novel therapeutic strategies. Immune checkpoint inhibitors, such as PD-1/PD-L1 antibodies, have been successfully loaded into nanocarriers and administered in combination with chemotherapeutic agents like doxorubicin or paclitaxel. This dual-delivery approach not only enhances cytotoxic killing but also reprograms the tumor immune microenvironment, improving infiltration of cytotoxic T cells and reducing immunosuppressive signaling [22]. Several preclinical models have demonstrated synergistic effects, and early-phase clinical trials conducted between 2019 and 2024 have confirmed improved response rates in patients with metastatic TNBC, particularly when checkpoint inhibitor-loaded nanocarriers were combined with conventional chemotherapy.Artificial intelligence has further strengthened breast cancer nanomedicine by enabling the discovery of predictive biomarkers [23]. Machine learning models trained on circulating tumor DNA (ctDNA), exosomal RNA, and proteomic datasets have been able to stratify patients according to likelihood of response to specific nanotherapies. For example, AI systems that integrate ctDNA mutational profiles with immune cell infiltration data have guided the selection of patients for nano-immunotherapy, improving trial efficiency and reducing the risk of non-responsiveness.Clinical progress has been particularly encouraging in TNBC, where several nano-immunotherapy trials initiated between 2019 and 2024 demonstrated durable responses in patients with advanced disease [24-25]. HER2+ and ER+ cohorts have also benefited from nano-enhanced targeted therapies, though these remain at earlier stages of clinical validation compared to TNBC. Collectively, these advances highlight how the convergence of nanomedicine and AI-driven biomarker discovery is not only reshaping the therapeutic landscape of breast cancer but also laying the groundwork for a truly personalized and subtype-specific treatment paradigm [26]. **(Figure 3)**

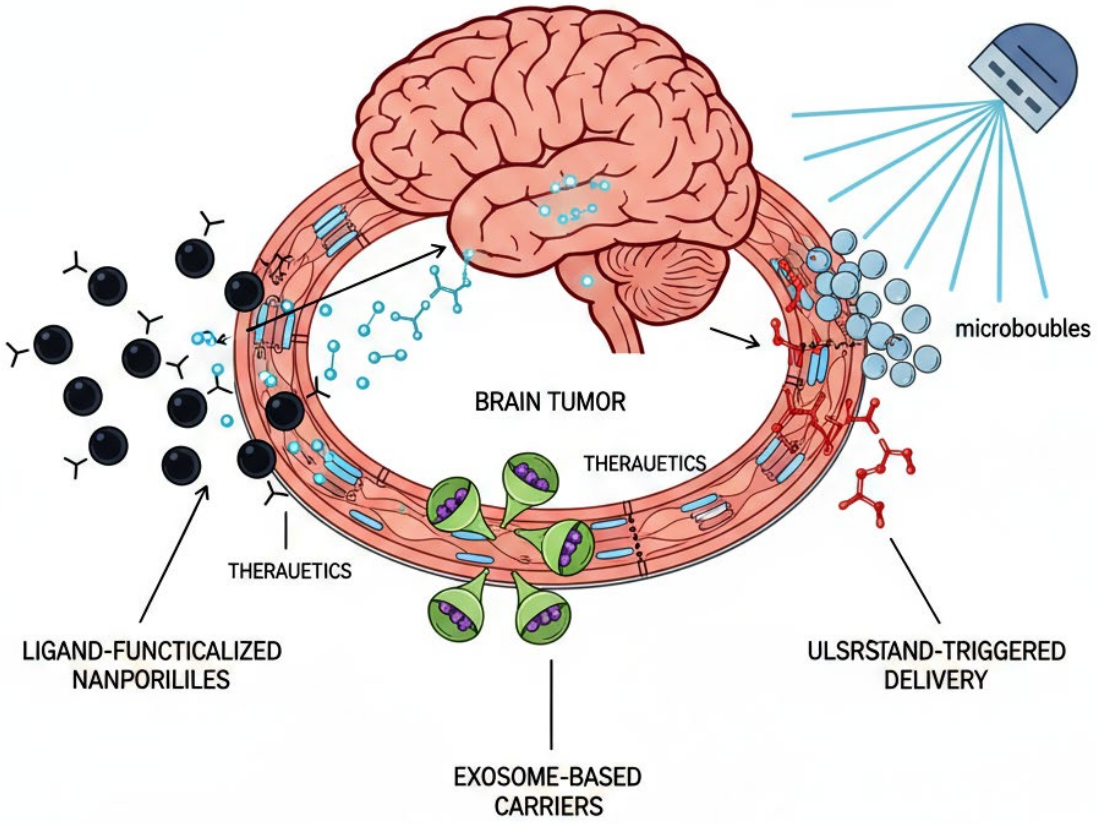

Figure 3: Overcoming the BBB.(Illustrate ligand-functionalized nanoparticle, exosome, and ultrasound-triggered delivery crossing the BBB.

5. Renal Cell Carcinoma (RCC)

Renal cell carcinoma presents unique therapeutic challenges due to its highly vascular and immunosuppressive tumor microenvironment. Recent nanomedicine strategies have focused on engineering carriers to penetrate hypoxic niches and disrupt stromal barriers that shield tumor cells from immune surveillance. Nanoparticles delivering VEGF inhibitors, tyrosine kinase inhibitors (TKIs), and immunomodulators have demonstrated improved bioavailability and reduced systemic toxicity compared to conventional formulations [27]. The integration of artificial intelligence has further refined these approaches by analyzing genomic and angiogenesis-related biomarkers, such as VHL mutations, to distinguish likely responders from non-responders. Despite these advances,

translation into clinical practice remains limited, as the heterogeneous vascularization and intrinsic drug resistance of RCC continue to hinder consistent therapeutic efficacy [28].

6. Neuro-Oncology (Glioblastoma and Beyond)

Glioblastoma and other central nervous system (CNS) malignancies remain among the most treatment-resistant cancers, largely due to the formidable blood–brain barrier (BBB). Recent advances in nanomedicine have introduced ligand-functionalized nanoparticles, exosome-based carriers, and ultrasound-triggered systems that enhance drug penetration into the brain [29]. In parallel, nano-immunotherapy has emerged as a promising frontier, with AI-assisted design of nanovaccines and checkpoint inhibitor–loaded particles demonstrating potential to reprogram the glioma immune microenvironment. Omics-guided strategies are increasingly integrated into these approaches, with biomarkers such as IDH mutations, MGMT methylation status, and immune profiling feeding into AI models for precise patient stratification. While several early-phase clinical trials highlight the promise of these strategies, challenges related to scalability, reproducibility, and long-term safety remain critical barriers to widespread clinical translation [30].

7. Future Perspectives

Looking ahead, the next phase of precision oncology will be shaped by the convergence of artificial intelligence, nanomedicine, and multi-omics technologies. One of the most promising directions is the AI-guided design of nanotherapeutics, where real-time simulations and generative models will allow rapid prototyping of nanoparticles with optimized pharmacokinetics, biodistribution, and payload compatibility [31]. This computational acceleration could shorten the timeline from bench discovery to clinical testing, dramatically increasing the adaptability of nanomedicine. At the same time, omics-driven personalization is expected to evolve into adaptive therapy pipelines, integrating genomics, transcriptomics, and proteomics into dynamic “digital twins” of patients. These models will enable therapy planning that continuously adapts to tumor evolution and resistance mechanisms [32].Global clinical adoption will also depend on seamless integration of nanomedicine with electronic health records (EHRs) and real-world data, allowing clinicians to match patients with tailored nanoformulations based on molecular profiles and historical treatment outcomes. Such integration could reduce disparities between trial results and actual clinical effectiveness [33]. However, with these technological leaps come significant ethical and regulatory responsibilities. Ensuring equitable access to AI-enabled nanotherapies, validating long-term safety across diverse populations, and maintaining transparency in algorithmic decision-making will be essential to secure patient trust and widespread adoption. Ultimately, the future of cancer nanomedicine lies in building systems that are not only technologically advanced but also clinically practical, ethically grounded, and globally scalable [34-35].

8. Conclusion

The era of AI-integrated nanomedicine is transforming oncology by introducing precision strategies that overcome the limitations of conventional therapies. Through the convergence of multi-omics insights and intelligent nanocarrier design, this paradigm is advancing toward personalized, adaptive, and durable treatment modalities. Although challenges such as translational hurdles, scalability, and long-term safety validation persist, the accelerating pace of innovation suggests that smart Nano medicine will soon become a cornerstone of modern oncology, shaping the future of cancer care.

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