EURASIAN EXPERIMENT JOURNAL OF BIOLOGICAL SCIENCES (EEJBS)
ISSN: 2992-4138 ©EEJBS Publications
Volume 6 Issue 3 2025

Nanotechnology in Cancer Immunotherapy: Emerging Strategies and Clinical Applications

Nyiramana Mukamurera P.

Faculty of Medicine Kampala International University Uganda

ABSTRACT

Cancer immunotherapy has revolutionized oncology by harnessing the body's immune system to combat malignant cells. Despite its success, challenges such as immune evasion, limited response rates, systemic toxicity, and tumor heterogeneity hinder its broader efficacy. Nanotechnology offers innovative solutions to these limitations through the design of versatile, biocompatible nanocarriers that enhance immune response, promote tumor-specific delivery, and reduce off-target effects. This review provides a comprehensive overview of the integration of nanotechnology with immunotherapy, highlighting emerging strategies including nanovaccines, immune checkpoint blockade delivery systems, nanocarriers for cytokine therapy, and nanoparticle-mediated T-cell modulation. It also discusses the recent advances in clinical trials and FDA-approved nano-immunotherapeutics, with an emphasis on safety, efficacy, and translational potential. Finally, the article explores current challenges and future directions in the field, suggesting that nanotechnology will continue to play a pivotal role in advancing personalized and more effective cancer immunotherapy strategies.

Keywords: Nanoparticles**;** Cancer Immunotherapy**;** Immune Checkpoint Inhibitors**;** Nanovaccines**;** Tumor Microenvironment

INTRODUCTION

Cancer continues to be one of the most significant global health challenges, accounting for millions of deaths annually and posing a considerable burden on healthcare systems worldwide[1–3]. Conventional treatment modalities surgery, chemotherapy, and radiation have contributed significantly to cancer management. However, these approaches often suffer from limitations such as nonspecific cytotoxicity[4], development of multidrug resistance, recurrence, and severe systemic side effects. These shortcomings underscore the urgent need for innovative, precise, and more effective therapeutic strategies. In recent years, cancer immunotherapy has revolutionized the oncology field by harnessing the patient's immune system to identify and eradicate malignant cells[4–6]. Unlike traditional therapies that act directly on tumors, immunotherapy empowers immune cells to recognize and attack cancer cells, offering durable and often curative outcomes in some cancers. Landmark immunotherapies—such as immune checkpoint inhibitors (e.g., anti-PD-1, anti-CTLA-4), chimeric antigen receptor (CAR) T-cell therapy, and cancer vaccines—have yielded unprecedented clinical responses, particularly in hematological malignancies and select solid tumors[7]. Despite these successes, the broad efficacy of immunotherapy remains hindered by several challenges. The tumor microenvironment (TME) often develops sophisticated mechanisms to evade immune surveillance, including secretion of immunosuppressive cytokines, recruitment of regulatory T cells (Tregs), and expression of checkpoint proteins[7]. Additionally, the poor immunogenicity of certain tumors, systemic toxicity from immune overactivation, and suboptimal delivery of immunotherapeutic agents all limit clinical outcomes.

Nanotechnology, the design and manipulation of materials at the nanometer scale (1–1000 nm) has emerged as a promising adjunct to overcome the limitations of current immunotherapeutic strategies[8–10]. Nanoparticles offer multiple advantages: they can be engineered for targeted delivery of immunomodulatory agents, protect biologics such as antibodies or mRNA from enzymatic degradation, and ensure sustained or stimuli-responsive release at tumor sites[11–13]. Moreover, nanocarriers can exploit the enhanced permeability and retention (EPR) effect a hallmark of solid tumors characterized by leaky vasculature and impaired lymphatic drainage to preferentially accumulate in tumor tissues while sparing healthy organs[10, 14, 15]. This enhances the therapeutic index and minimizes off-target effects. Beyond passive targeting, active targeting strategies can be

employed by functionalizing nanoparticles with ligands such as antibodies, peptides, or aptamers that specifically bind to overexpressed receptors on cancer cells or immune components. Additionally, nanoplatforms facilitate the co-delivery of multiple agents, such as antigens and adjuvants in cancer vaccines or combination therapies involving checkpoint inhibitors and cytokines, enabling synergistic therapeutic effects[16]. Certain nanomaterials themselves possess immunostimulatory properties, further enhancing their utility in immunotherapy. This review explores the convergence of nanotechnology and cancer immunotherapy, focusing on how engineered nanomaterials are reshaping the immunotherapeutic landscape. It delves into preclinical studies that demonstrate enhanced efficacy of nano-enabled immunotherapies, outlines the mechanistic insights into nanocarrier–immune system interactions, and surveys ongoing clinical trials and approved nanomedicines in this realm. Additionally, we discuss the challenges of nanotoxicity, immune compatibility, and regulatory hurdles that need to be addressed for widespread clinical adoption. The synergistic integration of nanotechnology with immunotherapy not only holds promise for improved therapeutic outcomes but also paves the way toward personalized and precision medicine in oncology.

2. Overview of Cancer Immunotherapy

Cancer immunotherapy represents a paradigm shift in oncology, wherein the immune system is modulated or activated to recognize and destroy tumor cells[17, 18]. Unlike conventional therapies that exert direct cytotoxic effects, immunotherapy aims to recalibrate the host immune response for sustained and selective anti-tumor activity. Broadly, immunotherapeutic strategies include immune checkpoint inhibitors (ICIs), adoptive cell therapy (ACT), cancer vaccines, and cytokine-based therapies. Each approach has shown varying degrees of success and faces unique challenges.

Immune checkpoint inhibitors (such as anti-PD-1, anti-PD-L1, and anti-CTLA-4 antibodies) block inhibitory signals that suppress T-cell activation, thereby enhancing the immune response against tumors [17, 19, 20]. These agents have achieved notable clinical successes in melanoma, non-small cell lung cancer (NSCLC), renal cell carcinoma, and more. However, not all patients respond, and immune-related adverse events (irAEs) such as colitis, pneumonitis, and dermatitis remain significant limitations[21, 22]. Adoptive cell therapy, particularly CAR-T cell therapy, involves ex vivo genetic modification of a patient's T cells to express chimeric receptors that recognize tumor antigens. While CAR-T therapy has revolutionized treatment for certain leukemias and lymphomas, its application in solid tumors is less effective due to the hostile TME, antigen heterogeneity, and on-target off-tumor toxicity[21].

Cancer vaccines aim to prime the immune system against tumor-associated antigens (TAAs) or neoantigens[23, 24]. They may be composed of peptides, DNA/RNA, dendritic cells, or whole tumor lysates. However, traditional vaccines often fail to elicit robust cytotoxic T-cell responses due to inadequate antigen presentation or immune suppression.

Cytokine therapy, using agents like interleukin-2 (IL-2) or interferon-alpha, can enhance immune activation. Nevertheless, systemic cytokine administration often leads to severe toxicity and limited efficacy, necessitating more targeted delivery systems. One of the primary barriers to effective immunotherapy is the tumor microenvironment (TME)[19, 25, 26]. The TME consists of a complex interplay of tumor cells, stromal components, immune suppressive cells (e.g., Tregs, myeloid-derived suppressor cells), and cytokines that collectively inhibit immune activation. Additionally, therapeutic biomolecules often suffer from poor bioavailability, short half-lives, and limited penetration into tumor tissues[27–29].

This is where nanotechnology plays a transformative role. Nanocarriers—liposomes, polymeric nanoparticles, dendrimers, micelles, exosomes, and inorganic nanoparticles—can be engineered to shield immunotherapeutics from premature degradation in circulation, prolong their half-lives, and improve tumor-specific delivery via both passive (EPR effect) and active targeting[8, 9, 30]. For instance, nanoparticles can encapsulate ICIs, preventing systemic exposure and releasing them selectively within the TME. Likewise, they can be loaded with tumor antigens and adjuvants for co-delivery in cancer vaccines, enhancing antigen presentation and T-cell priming[31]. Moreover, nanocarriers can modulate the immune system directly. Some nanomaterials serve as adjuvants, stimulating innate immune pathways such as Toll-like receptors (TLRs). Others can reprogram the TME by delivering immunostimulatory cytokines, depleting suppressive cells, or normalizing tumor vasculature to enhance T-cell infiltration[31].

In sum, while cancer immunotherapy has revolutionized treatment, its full potential remains untapped due to multiple biological and pharmacological barriers. The incorporation of nanotechnology offers a multifaceted solution, improving pharmacokinetics, reducing toxicity, enhancing immune engagement, and overcoming resistance mechanisms. The synergy between these fields is poised to usher in a new era of precision immuno-oncology. This review continues by dissecting specific nano-enabled immunotherapies and their clinical relevance.

3. Nanotechnology-Enabled Strategies in Cancer Immunotherapy

3.1. Nanovaccines: Nanovaccines represent a promising frontier in cancer immunotherapy by harnessing nanoscale delivery systems to enhance antigen presentation and immune activation[32, 33]. These formulations consist of nanoparticles encapsulating tumor-specific antigens and often include adjuvants to further stimulate the immune response. By targeting dendritic cells (DCs) and other antigen-presenting cells (APCs), nanovaccines facilitate efficient antigen uptake and cross-presentation via MHC class I and II pathways, leading to the activation of cytotoxic CD8+ T lymphocytes and helper CD4+ T cells. The nanoscale size improves lymphatic drainage and enables efficient trafficking to lymph nodes where immune priming occurs[34]. Various nanomaterials, including lipid-based nanoparticles (such as liposomes), polymeric nanoparticles (e.g., PLGA), and self-assembling peptide nanostructures, have been utilized to develop nanovaccines for a range of cancers, including melanoma, lung, and breast cancer[34]. These platforms offer superior stability, controlled release, and the potential for multivalent antigen presentation, thereby improving the immunogenicity and therapeutic potential of cancer vaccines.

3.2. Nanoparticles for Immune Checkpoint Inhibitors: Immune checkpoint blockade has revolutionized cancer therapy, but the systemic delivery of monoclonal antibodies targeting PD-1, PD-L1, or CTLA-4 often results in dose-limiting immune-related adverse effects[35]. Nanoparticles provide an effective strategy to overcome these limitations by enabling localized and targeted delivery of immune checkpoint inhibitors to the tumor microenvironment (TME). Engineered nanocarriers, such as lipid nanoparticles, polymeric vesicles, and dendrimers, can encapsulate or surface-functionalize checkpoint inhibitors, ensuring their accumulation in tumors through the enhanced permeability and retention (EPR) effect or active targeting ligands[36]. This targeted approach reduces systemic toxicity and improves therapeutic index. Additionally, nanoparticles can be co-loaded with synergistic agents, such as Toll-like receptor (TLR) agonists or cytokines, to amplify the immune response[36]. For example, co-delivery of anti-PD-1 antibodies with tumor antigens or immunostimulatory molecules can enhance T cell infiltration and activation, offering a combinatorial immunotherapeutic approach for solid tumors that are otherwise resistant to checkpoint blockade[37].

3.3. Nanocarriers for Cytokine Delivery: Cytokines are powerful immune modulators with significant potential in cancer immunotherapy; however, their clinical utility is hampered by rapid degradation, poor pharmacokinetics, and systemic toxicity[38]. Nanocarrier-based delivery systems provide a solution by encapsulating cytokines like interleukin-2 (IL-2), interleukin-12 (IL-12), and interferon-gamma (IFN-γ), allowing for sustained, controlled, and localized release at tumor sites. These platforms improve cytokine stability and bioavailability while minimizing off-target effects. Liposomes, hydrogels, dendritic polymers, and biodegradable nanoparticles such as PLGA and PEG-based systems have been successfully employed for cytokine delivery[39, 40]. Furthermore, these carriers can be engineered to respond to tumor-specific stimuli (e.g., acidic pH, enzymes) to ensure on-demand release, enhancing their safety and efficacy profiles. This targeted approach not only activates immune cells such as T lymphocytes and natural killer (NK) cells but also modulates the immunosuppressive tumor microenvironment, thereby promoting robust and durable antitumor immune responses while avoiding the systemic toxicity commonly seen with free cytokine therapy[41].

3.4. Nanoparticle-Mediated T-cell Modulation: Nanoparticles offer novel strategies to directly modulate T-cell function, thereby enhancing the efficacy of adoptive cell therapies and in situ immune responses against tumors. One approach involves artificial antigen-presenting cell (aAPC)-mimetic nanoparticles that present specific tumor antigens along with co-stimulatory signals to prime naïve or memory T cells [42]. These nanocarriers can be used ex vivo to expand tumor-specific T cells before reinfusion or administered in vivo to stimulate T cells directly within the body. Moreover, nanoparticles can deliver genetic tools such as CRISPR-Cas9 or siRNA to T cells, enabling gene editing to enhance T-cell persistence, reduce exhaustion, or engineer resistance to the immunosuppressive tumor microenvironment[43, 44]. Other formulations may transport metabolic modulators or checkpoint inhibitors specifically to T cells to sustain their activation and cytotoxicity. By refining T-cell phenotype, trafficking, and functionality, nanoparticle-mediated strategies represent a cutting-edge approach to overcoming immune evasion and achieving long-lasting antitumor immunity.

4. Modulating the Tumor Microenvironment with Nanotechnology

The tumor microenvironment (TME) is a complex and dynamic ecosystem composed of cancer cells, stromal cells, immune cells, extracellular matrix components, and a range of cytokines and growth factors[29, 45, 46]. One of the key challenges in effective cancer immunotherapy is the immunosuppressive nature of the TME, which hampers the infiltration, activation, and function of immune effector cells. Nanotechnology offers innovative approaches to remodel the TME and shift it from an immunosuppressive to an immunostimulatory state, thereby enhancing therapeutic efficacy.

Nanoparticles (NPs) can be engineered to deliver immunomodulatory agents directly to the TME. This site-specific delivery increases local drug concentration, reduces systemic toxicity, and ensures targeted action. For example, inhibitors of indoleamine 2,3-dioxygenase (IDO)—an enzyme that depletes tryptophan and suppresses

T-cell activity can be encapsulated in nanoparticles and selectively delivered to the tumor site. This strategy restores T-cell function and reduces immune escape by tumor cells[47–49]. Another critical component of the immunosuppressive TME is the presence of regulatory T cells (Tregs), which inhibit cytotoxic T lymphocytes and natural killer (NK) cells. Nanocarriers can be used to deliver agents such as cyclophosphamide or anti-CD25 antibodies that selectively deplete Tregs within tumors, thereby unblocking immune surveillance mechanisms. Similarly, immune checkpoint inhibitors like anti-PD-1 or anti-CTLA-4 can be co-delivered with Treg-depleting agents in multifunctional nanoparticles, offering a synergistic therapeutic outcome.

Tumor-associated macrophages (TAMs) represent another targetable cell population in the TME. TAMs predominantly exhibit an M2-like phenotype associated with tissue repair and immune suppression. Reprogramming these macrophages to an M1-like phenotype associated with pro-inflammatory and antitumor activities can substantially enhance immune-mediated tumor destruction[50]. Nanoparticles loaded with TLR agonists, STAT3 inhibitors, or other repolarizing agents can induce this phenotypic switch, transforming TAMs from tumor-promoting to tumor-fighting cells. Moreover, nanoparticles can modulate the TME by disrupting stromal barriers and enhancing the infiltration of immune cells[50]. For instance, hyaluronidase-loaded NPs degrade hyaluronic acid in the extracellular matrix, improving T-cell access to tumor cells. Other nanocarriers can deliver siRNA or CRISPR components to downregulate genes involved in immune evasion, such as PD-L1 or VEGF[51].

By combining TME-targeted approaches with antigen delivery systems and immune checkpoint blockade, nanotechnology enables a comprehensive remodeling of the tumor milieu. This multi-pronged strategy not only sensitizes tumors to immunotherapy but also facilitates durable and systemic anti-tumor responses[51]. The integration of nanomedicine into TME modulation represents a transformative shift in cancer immunotherapy, offering the potential to convert "cold" tumors, those lacking immune infiltration, into "hot" tumors responsive to immune intervention.

5. Clinical Applications and Translational Progress

The application of nanotechnology in cancer immunotherapy has transitioned from preclinical promise to early clinical validation, with several formulations progressing through clinical trials[52]. These advances mark a significant shift in how nanomedicine is being harnessed to modulate immune responses and enhance cancer treatment outcomes. Although regulatory approval remains limited, the clinical pipeline of nano-immunotherapeutics continues to grow, underscoring their translational potential. A prominent example is NBTXR3, a hafnium oxide nanoparticle developed as a radioenhancer[53]. Upon intratumoral injection and exposure to ionizing radiation, NBTXR3 amplifies radiation-induced DNA damage in cancer cells while also promoting the release of tumor antigens. This process facilitates dendritic cell activation and subsequent T-cell priming, effectively linking radiotherapy with immune activation. Clinical trials are ongoing for multiple cancers, including head and neck squamous cell carcinoma and soft tissue sarcoma[53].

Another notable candidate is BNT111, a liposomal mRNA nanovaccine targeting four melanoma-associated antigens: NY-ESO-1, MAGE-A3, tyrosinase, and TPTE. Developed by BioNTech, BNT111 is currently in Phase II clinical trials and is designed to stimulate strong CD4+ and CD8+ T-cell responses[54]. This nanovaccine exemplifies how mRNA encapsulation in lipid nanoparticles (LNPs), as seen in COVID-19 vaccines, can be repurposed for oncology, paving the way for rapid and personalized cancer immunotherapies.

Moreover, nanotechnology is increasingly used to enhance the delivery of immune checkpoint inhibitors. For example, anti-PD-1 and anti-CTLA-4 antibodies can be co-delivered with immunomodulators or tumor antigens using biodegradable polymeric nanoparticles. These formulations offer sustained drug release, reduced systemic toxicity, and improved therapeutic synergy[54]. Despite these promising developments, regulatory approval for nano-immunotherapies remains limited. Only a few nanoparticle-based cancer therapies—such as Abraxane® (albumin-bound paclitaxel) and Doxil® (pegylated liposomal doxorubicin) have received FDA approval, and they primarily function via cytotoxic mechanisms rather than immune modulation[55]. The gap between innovation and regulatory approval stems from several challenges: establishing long-term safety profiles, demonstrating consistent clinical efficacy, and scaling up manufacturing under Good Manufacturing Practices (GMP)[55].

Nonetheless, the increasing interest and investment in nanotechnology-driven immunotherapy are encouraging. The use of companion diagnostics, biomarker-guided trials, and AI-assisted drug design is accelerating the clinical translation of nanomedicines. Additionally, advances in personalized medicine and genomic profiling enable tailored nanovaccine development based on individual tumor antigen signatures.

In sum, while the clinical application of nano-immunotherapies is still in its nascent stages, their potential to revolutionize cancer treatment is evident. Continued interdisciplinary collaboration and regulatory innovation will be essential to bring these next-generation therapies to the clinic and ultimately to the patient's bedside.

6. Challenges and Future Perspectives

Despite the growing promise of nanotechnology in cancer immunotherapy, several scientific, technical, and clinical challenges must be addressed to fully realize its potential. These limitations span nanoparticle design, biological interactions, manufacturing, and patient-specific considerations, all of which impact therapeutic efficacy and regulatory approval.

One of the most pressing issues is nanotoxicity. Although many nanomaterials are designed to be biocompatible and biodegradable, their interactions with biological systems can result in unforeseen side effects. Accumulation in non-target organs such as the liver, spleen, or kidneys may induce inflammatory responses, oxidative stress, or organ damage. Additionally, some inorganic nanomaterials (e.g., gold, silver, carbon-based nanostructures) exhibit poor biodegradability, raising concerns about long-term retention and safety. Comprehensive toxicological assessments, including both acute and chronic exposure studies, are essential before clinical application.

Variability in biodistribution and pharmacokinetics also poses a major hurdle. Nanoparticles often exhibit heterogeneous accumulation in tumors due to differences in vascular permeability, interstitial pressure, and lymphatic drainage between patients or even between tumors within the same individual. This variability challenges consistent dosing and therapeutic outcomes, necessitating the development of smart or responsive nanocarriers that adapt to the tumor microenvironment.

Manufacturing and scalability represent additional bottlenecks. The reproducible synthesis of nanoparticles with precise size, shape, surface charge, and functionalization is technically demanding. Small variations in these parameters can significantly alter biodistribution and immune responses. Ensuring batch-to-batch consistency under GMP conditions while keeping production cost-effective is vital for commercial viability and regulatory approval.

Another critical challenge lies in the patient-specific nature of immune responses**.** Genetic, epigenetic, and environmental factors influence how an individual's immune system reacts to both cancer and immunotherapies. Thus, a "one-size-fits-all" approach to nano-immunotherapy may be suboptimal. Integrating personalized medicine strategies—such as genomic profiling, tumor mutational burden assessment, and immune cell phenotyping—can help tailor nanoparticle formulations to individual patient immunoprofiles.

Looking ahead, artificial intelligence (AI) and machine learning (ML) hold promise for optimizing nanoparticle design and predicting therapeutic outcomes. AI algorithms can identify optimal combinations of particle size, shape, and surface chemistry based on large datasets, accelerating the design of next-generation nanomedicines. Similarly, AI-driven analysis of patient data can guide treatment decisions and improve response prediction.

Future perspectives also include the development of multifunctional nanoplatforms capable of simultaneous diagnosis, therapy, and real-time monitoring, so-called "theranostics." Such systems could revolutionize cancer management by allowing early detection, precise treatment, and continuous evaluation of therapeutic response.

While challenges remain, the future of nanotechnology in cancer immunotherapy is bright. Overcoming current barriers through multidisciplinary collaboration, regulatory adaptation, and technological innovation will pave the way for safe, effective, and personalized nano-immunotherapies in oncology.

CONCLUSION

Nanotechnology is poised to transform the landscape of cancer immunotherapy by enabling precise, potent, and personalized treatment strategies. From enhancing vaccine efficacy to overcoming immune resistance in the TME, nanocarriers provide a versatile platform for next-generation immunotherapeutics. Continued interdisciplinary research and clinical validation are essential to harness the full potential of this synergistic approach and bring novel treatments to patients worldwide.

REFERENCES

1. Abbas, Z., Rehman, S., Abbas, Z., Rehman, S.: An Overview of Cancer Treatment Modalities. In: Neoplasm. IntechOpen (2018)
2. Abedi-Gaballu, F., Dehghan, G., Ghaffari, M., Yekta, R., Abbaspour-Ravasjani, S., Baradaran, B., Dolatabadi, J.E.N., Hamblin, M.R.: PAMAM dendrimers as efficient drug and gene delivery nanosystems for cancer therapy. Appl Mater Today. 12, 177–190 (2018). https://doi.org/10.1016/j.apmt.2018.05.002
3. Abolhassani, H., Eskandari, A., Saremi Poor, A., Zarrabi, A., Khodadadi, B., Karimifard, S., Sahrayi, H., Bourbour, M., Tavakkoli Yaraki, M.: Nanobiotechnological approaches for breast cancer Management: Drug delivery systems and 3D In-Vitro models. Coordination Chemistry Reviews. 508, 215754 (2024). https://doi.org/10.1016/j.ccr.2024.215754
4. Zafar, A., Khatoon, S., Khan, M.J., Abu, J., Naeem, A.: Advancements and limitations in traditional anti-cancer therapies: a comprehensive review of surgery, chemotherapy, radiation therapy, and hormonal therapy. Discov Oncol. 16, 607 (2025). https://doi.org/10.1007/s12672-025-02198-8
5. Alum, E.U.: AI-driven biomarker discovery: enhancing precision in cancer diagnosis and prognosis. Discov Onc. 16, 313 (2025). https://doi.org/10.1007/s12672-025-02064-7

6. Alum, E.U., Akwari, A.Ak., Okoroh, P.N., Aniokete, U.C., Abba, J.N., Uti, D.E.: Phytochemicals as modulators of ferroptosis: a novel therapeutic avenue in cancer and neurodegeneration. Mol Biol Rep. 52, 636 (2025). https://doi.org/10.1007/s11033-025-10752-4
7. Shiravand, Y., Khodadadi, F., Kashani, S.M.A., Hosseini-Fard, S.R., Hosseini, S., Sadeghirad, H., Ladwa, R., O'Byrne, K., Kulasinghe, A.: Immune Checkpoint Inhibitors in Cancer Therapy. Curr Oncol. 29, 3044–3060 (2022). https://doi.org/10.3390/curroncol29050247
8. Alghamdi, M.A., Fallica, A.N., Virzì, N., Kesharwani, P., Pittalà, V., Greish, K.: The Promise of Nanotechnology in Personalized Medicine. J Pers Med. 12, 673 (2022). https://doi.org/10.3390/jpm12050673
9. Anjum, S., Ishaque, S., Fatima, H., Farooq, W., Hano, C., Abbasi, B.H., Anjum, I.: Emerging Applications of Nanotechnology in Healthcare Systems: Grand Challenges and Perspectives. Pharmaceuticals (Basel). 14, 707 (2021). https://doi.org/10.3390/ph14080707
10. Alum, E.U., Nwuruku, O.A., Ugwu, O.P.-C., Uti, D.E., Alum, B.N., Edwin, N.: Harnessing nature: plant-derived nanocarriers for targeted drug delivery in cancer therapy. Phytomedicine Plus. 5, 100828 (2025). https://doi.org/10.1016/j.phyplu.2025.100828
11. Hetta, H.F., Ramadan, Y.N., Al-Harbi, A.I., A. Ahmed, E., Battah, B., Abd Ellah, N.H., Zanetti, S., Donadu, M.G.: Nanotechnology as a Promising Approach to Combat Multidrug Resistant Bacteria: A Comprehensive Review and Future Perspectives. Biomedicines. 11, 413 (2023). https://doi.org/10.3390/biomedicines11020413
12. Krsek, A., Baticic, L.: Nanotechnology-Driven Therapeutic Innovations in Neurodegenerative Disorders: A Focus on Alzheimer's and Parkinson's Disease. Future Pharmacology. 4, 352–379 (2024). https://doi.org/10.3390/futurepharmacol4020020
13. Uti, D.E., Atangwho, I.J., Alum, E.U., Ntaobeten, E., Obeten, U.N., Bawa, I., Agada, S.A., Ukam, C.I.-O., Egbung, G.E.: Antioxidants in cancer therapy mitigating lipid peroxidation without compromising treatment through nanotechnology. Discover Nano. 20, 70 (2025). https://doi.org/10.1186/s11671-025-04248-0
14. Teixeira, M.I., Lopes, C.M., Amaral, M.H., Costa, P.C.: Surface-modified lipid nanocarriers for crossing the blood-brain barrier (BBB): A current overview of active targeting in brain diseases. Colloids and Surfaces B: Biointerfaces. 221, 112999 (2023). https://doi.org/10.1016/j.colsurfb.2022.112999
15. Milewska, S., Niemirowicz-Laskowska, K., Siemiaszko, G., Nowicki, P., Wilczewska, A.Z., Car, H.: Current Trends and Challenges in Pharmacoeconomic Aspects of Nanocarriers as Drug Delivery Systems for Cancer Treatment. Int J Nanomedicine. 16, 6593–6644 (2021). https://doi.org/10.2147/IJN.S323831
16. Uti, D.E., Alum, E.U., Atangwho, I.J., Ugwu, O.P.-C., Egbung, G.E., Aja, P.M.: Lipid-based nano-carriers for the delivery of anti-obesity natural compounds: advances in targeted delivery and precision therapeutics. Journal of Nanobiotechnology. 23, 336 (2025). https://doi.org/10.1186/s12951-025-03412-z
17. Almohaimeed, H.M., Chowdhury, A., Sarkar, S., Almars, A.I., Tounsi, W.A., Singh, A., Krithiga, T., Ray, S., Uti, D.Ej.: Advances in cancer immunotherapy: The role of super NK and super CAR-T cells. Int Immunopharmacol. 161, 115074 (2025). https://doi.org/10.1016/j.intimp.2025.115074
18. Godakhindi, V., Tarannum, M., Dam, S.K., Vivero-Escoto, J.L.: Mesoporous Silica Nanoparticles as an Ideal Platform for Cancer Immunotherapy: Recent Advances and Future Directions. Advanced Healthcare Materials. 13, 2400323 (2024). https://doi.org/10.1002/adhm.202400323
19. Yang, Y., Li, S., To, K.K.W., Zhu, S., Wang, F., Fu, L.: Tumor-associated macrophages remodel the suppressive tumor immune microenvironment and targeted therapy for immunotherapy. J Exp Clin Cancer Res. 44, 145 (2025). https://doi.org/10.1186/s13046-025-03377-9
20. Xu, R., Lin, P., Zheng, J., Lin, Y., Mai, Z., Lu, Y., Chen, X., Zhou, Z., Cui, L., Zhao, X.: Orchestrating cancer therapy: Recent advances in nanoplatforms harmonize immunotherapy with multifaceted treatments. Materials Today Bio. 30, 101386 (2025). https://doi.org/10.1016/j.mtbio.2024.101386
21. Dela Cruz, Ma.C.P., Medina, P.M.B.: Epithelial-mesenchymal transition (EMT) and its role in acquired epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) chemoresistance in non-small cell lung cancer (NSCLC). Cancer Pathogenesis and Therapy. 03, 215–225 (2025). https://doi.org/10.1016/j.cpt.2024.07.001
22. Mina, S.A., Shanshal, M., Leventakos, K., Parikh, K.: Emerging Targeted Therapies in Non-Small-Cell Lung Cancer (NSCLC). Cancers. 17, 353 (2025). https://doi.org/10.3390/cancers17030353
23. Çetinkaya, M., Baran, Y.: Therapeutic Potential of Luteolin on Cancer. Vaccines (Basel). 11, 554 (2023). https://doi.org/10.3390/vaccines11030554

24. Jiang, Y., Chen, M., Nie, H., Yuan, Y.: PD-1 and PD-L1 in cancer immunotherapy: clinical implications and future considerations. Hum Vaccin Immunother. 15, 1111–1122 (2019). https://doi.org/10.1080/21645515.2019.1571892
25. Chen, X., Zheng, Y., Zhang, Q., Chen, Q., Chen, Z., Wu, D.: Dual-targeted delivery of temozolomide by multi-responsive nanoplatform via tumor microenvironment modulation for overcoming drug resistance to treat glioblastoma. Journal of Nanobiotechnology. 22, 264 (2024). https://doi.org/10.1186/s12951-024-02531-3
26. de Visser, K.E., Joyce, J.A.: The evolving tumor microenvironment: From cancer initiation to metastatic outgrowth. Cancer Cell. 41, 374–403 (2023). https://doi.org/10.1016/j.ccell.2023.02.016
27. Gu, X.-Y., Yang, J.-L., Lai, R., Zhou, Z.-J., Tang, D., Hu, L., Zhao, L.-J.: Impact of lactate on immune cell function in the tumor microenvironment: mechanisms and therapeutic perspectives. Front Immunol. 16, 1563303 (2025). https://doi.org/10.3389/fimmu.2025.1563303
28. Liu, Y., Si, L., Jiang, Y., Jiang, S., Zhang, X., Li, S., Chen, J., Hu, J.: Design of pH-Responsive Nanomaterials Based on the Tumor Microenvironment. Int J Nanomedicine. 20, 705–721 (2025). https://doi.org/10.2147/IJN.S504629
29. Huai, Y., Hossen, M.N., Wilhelm, S., Bhattacharya, R., Mukherjee, P.: Nanoparticle Interactions with the Tumor Microenvironment. Bioconjug Chem. 30, 2247–2263 (2019). https://doi.org/10.1021/acs.bioconjchem.9b00448
30. Ammar, M.M., Ali, R., Abd Elaziz, N.A., Habib, H., Abbas, F.M., Yassin, M.T., Maniah, K., Abdelaziz, R.: Nanotechnology in oncology: advances in biosynthesis, drug delivery, and theranostics. Discov Onc. 16, 1172 (2025). https://doi.org/10.1007/s12672-025-02664-3
31. Bishoyi, A.K., Nouri, S., Hussen, A., Bayani, A., Khaksari, M.N., Soleimani Samarkhazan, H.: Nanotechnology in leukemia therapy: revolutionizing targeted drug delivery and immune modulation. Clin Exp Med. 25, 166 (2025). https://doi.org/10.1007/s10238-025-01686-z
32. Lu, L., Duong, V.T., Shalash, A.O., Skwarczynski, M., Toth, I.: Chemical Conjugation Strategies for the Development of Protein-Based Subunit Nanovaccines. Vaccines (Basel). 9, 563 (2021). https://doi.org/10.3390/vaccines9060563
33. Priyanka, Abusalah, M.A.H., Chopra, H., Sharma, A., Mustafa, S.A., Choudhary, O.P., Sharma, M., Dhawan, M., Khosla, R., Loshali, A., Sundriyal, A., Saini, J.: Nanovaccines: A game changing approach in the fight against infectious diseases. Biomedicine & Pharmacotherapy. 167, 115597 (2023). https://doi.org/10.1016/j.biopha.2023.115597
34. Kim, C.G., Kye, Y.-C., Yun, C.-H.: The Role of Nanovaccine in Cross-Presentation of Antigen-Presenting Cells for the Activation of CD8+ T Cell Responses. Pharmaceutics. 11, 612 (2019). https://doi.org/10.3390/pharmaceutics11110612
35. Yao, M., Liu, X., Qian, Z., Fan, D., Sun, X., Zhong, L., Wu, P.: Research progress of nanovaccine in anti-tumor immunotherapy. Front Oncol. 13, 1211262 (2023). https://doi.org/10.3389/fonc.2023.1211262
36. Fallatah, M.M., Alradwan, I., Alfayez, N., Aodah, A.H., Alkhrayef, M., Majrashi, M., Jamous, Y.F.: Nanoparticles for Cancer Immunotherapy: Innovations and Challenges. Pharmaceuticals. 18, 1086 (2025). https://doi.org/10.3390/ph18081086
37. Tang, T., Huang, X., Zhang, G., Hong, Z., Bai, X., Liang, T.: Advantages of targeting the tumor immune microenvironment over blocking immune checkpoint in cancer immunotherapy. Signal Transduct Target Ther. 6, 72 (2021). https://doi.org/10.1038/s41392-020-00449-4
38. Fu, Y., Tang, R., Zhao, X.: Engineering cytokines for cancer immunotherapy: a systematic review. Front Immunol. 14, 1218082 (2023). https://doi.org/10.3389/fimmu.2023.1218082
39. Sousa, F., Lee, H., Almeida, M., Bazzoni, A., Rothen-Rutishauser, B., Petri-Fink, A.: Immunostimulatory nanoparticles delivering cytokines as a novel cancer nanoadjuvant to empower glioblastoma immunotherapy. Drug Deliv Transl Res. 14, 2655–2667 (2024). https://doi.org/10.1007/s13346-023-01509-2
40. Uti, D.E., Atangwho, I.J., Omang, W.A., Alum, E.U., Obeten, U.N., Udeozor, P.A., Agada, S.A., Bawa, I., Ogbu, C.O.: Cytokines as key players in obesity low grade inflammation and related complications. Obesity Medicine. 54, 100585 (2025). https://doi.org/10.1016/j.obmed.2025.100585
41. Sabit, H., Pawlik, T.M., Radwan, F., Abdel-Hakeem, M., Abdel-Ghany, S., Wadan, A.-H.S., Elzawahri, M., El-Hashash, A., Arneth, B.: Precision nanomedicine: navigating the tumor microenvironment for enhanced cancer immunotherapy and targeted drug delivery. Molecular Cancer. 24, 160 (2025). https://doi.org/10.1186/s12943-025-02357-z
42. Est-Witte, S.E., Livingston, N.K., Omotoso, M.O., Green, J.J., Schneck, J.P.: Nanoparticles for generating antigen-specific T cells for immunotherapy. Semin Immunol. 56, 101541 (2021). https://doi.org/10.1016/j.smim.2021.101541

43. Chen, Z., Krishnamachary, B., Pachecho-Torres, J., Penet, M.-F., Bhujwalla, Z.M.: Theranostic small interfering RNA nanoparticles in cancer precision nanomedicine. Wiley Interdiscip Rev Nanomed Nanobiotechnol. 12, e1595 (2020). https://doi.org/10.1002/wnan.1595
44. Bashir, S., Amn Zia, M., Shoukat, M., Kaleem, I., Bashir, S.: Nanoparticles as a novel key driver for the isolation and detection of circulating tumour cells. Sci Rep. 14, 22580 (2024). https://doi.org/10.1038/s41598-024-67221-4
45. Kozieł, M.J., Piastowska-Ciesielska, A.W.: Estrogens, Estrogen Receptors and Tumor Microenvironment in Ovarian Cancer. International Journal of Molecular Sciences. 24, 14673 (2023). https://doi.org/10.3390/ijms241914673
46. Labani-Motlagh, A., Ashja-Mahdavi, M., Loskog, A.: The Tumor Microenvironment: A Milieu Hindering and Obstructing Antitumor Immune Responses. Front Immunol. 11, 940 (2020). https://doi.org/10.3389/fimmu.2020.00940
47. Kuo, C.-L., Ponneri Babuharisankar, A., Lin, Y.-C., Lien, H.-W., Lo, Y.K., Chou, H.-Y., Tangeda, V., Cheng, L.-C., Cheng, A.N., Lee, A.Y.-L.: Mitochondrial oxidative stress in the tumor microenvironment and cancer immunoescape: foe or friend? Journal of Biomedical Science. 29, 74 (2022). https://doi.org/10.1186/s12929-022-00859-2
48. Issa, H., Singh, L., Lai, K.-S., Parusheva-Borsitzky, T., Ansari, S.: Dynamics of inflammatory signals within the tumor microenvironment. World J Exp Med. 15, 102285 (2025). https://doi.org/10.5493/wjem.v15.i2.102285
49. He, Q., Chen, J., Yan, J., Cai, S., Xiong, H., Liu, Y., Peng, D., Mo, M., Liu, Z.: Tumor microenvironment responsive drug delivery systems. Asian J Pharm Sci. 15, 416–448 (2020). https://doi.org/10.1016/j.ajps.2019.08.003
50. Wang, S., Wang, J., Chen, Z., Luo, J., Guo, W., Sun, L., Lin, L.: Targeting M2-like tumor-associated macrophages is a potential therapeutic approach to overcome antitumor drug resistance. NPJ Precis Oncol. 8, 31 (2024). https://doi.org/10.1038/s41698-024-00522-z
51. Ultimo, A., Jain, A., Gomez-Gonzalez, E., Alex, T.S., Moreno-Borrallo, A., Jana, S., Ghosh, S., Ruiz-Hernandez, E.: Nanotherapeutic Formulations for the Delivery of Cancer Antiangiogenics. Mol Pharm. 22, 2322–2349 (2025). https://doi.org/10.1021/acs.molpharmaceut.4c00822
52. Rashidi, N., Davidson, M., Apostolopoulos, V., Nurgali, K.: Nanoparticles in cancer diagnosis and treatment: Progress, challenges, and opportunities. Journal of Drug Delivery Science and Technology. 95, 105599 (2024). https://doi.org/10.1016/j.jddst.2024.105599
53. Samathoti, P., Kumarachari, R.K., Bukke, S.P.N., Rajasekhar, E.S.K., Jaiswal, A.A., Eftekhari, Z.: The role of nanomedicine and artificial intelligence in cancer health care: individual applications and emerging integrations—a narrative review. Discov Onc. 16, 697 (2025). https://doi.org/10.1007/s12672-025-02469-4
54. Lorentzen, C.L., Haanen, J.B., Met, Ö., Svane, I.M.: Clinical advances and ongoing trials of mRNA vaccines for cancer treatment. Lancet Oncol. 23, e450–e458 (2022). https://doi.org/10.1016/S1470-2045(22)00372-2
55. Venturini, J., Chakraborty, A., Baysal, M.A., Tsimberidou, A.M.: Developments in nanotechnology approaches for the treatment of solid tumors. Exp Hematol Oncol. 14, 76 (2025). https://doi.org/10.1186/s40164-025-00656-1

CITE AS: Nyiramana Mukamurera P. (2025). Nanotechnology in Cancer Immunotherapy: Emerging Strategies and Clinical Applications. EURASIAN EXPERIMENT JOURNAL OF BIOLOGICAL SCIENCES 6(3):45-52