NEWPORT INTERNATIONAL JOURNAL OF SCIENTIFIC AND EXPERIMENTAL SCIENCES (NIJSES)

Volume 6 Issue 3 Page 62-69, 2025

©NIJSES PUBLICATIONS
Open Access

ONLINE ISSN:2992-5819
PRINT ISSN:2992-6149

https://doi.org/10.59298/NIJSES/2025/63.6269

Exosome-Mimetic Nanoparticles in Cancer Immunotherapy: Mimicry, Modulation, and Delivery

Mpora Kakwanzi Evelyn

Department of Pharmacognosy Kampala International University Uganda
Email: evelyne.mpora@studwc.kiu.ac.ug

ABSTRACT

Cancer immunotherapy has revolutionized oncology, yet its success is limited by factors such as immunosuppressive tumor microenvironments, inadequate antigen presentation, and inefficient immune cell engagement. Exosome-mimetic nanoparticles (EMNs) have emerged as a promising biomimetic platform capable of overcoming these challenges. Derived from natural membranes or engineered to mimic exosomal features, EMNs retain the beneficial biological properties of exosomes, such as biocompatibility, immune modulation, and homing capability, while offering enhanced scalability, stability, and payload versatility. This review provides a comprehensive overview of the current state and future potential of EMNs in cancer immunotherapy. We discuss the principles of exosomal mimicry, their role in modulating immune responses, and their application as delivery vehicles for immune checkpoint inhibitors, cytokines, and tumor antigens. Furthermore, we explore engineering strategies for functionalization and tumor targeting, as well as recent preclinical advances and translational challenges. By bridging nanotechnology and immuno-oncology, EMNs hold immense potential to boost therapeutic efficacy and reshape the landscape of cancer treatment.

Keywords: Exosome-mimetic nanoparticles, cancer immunotherapy, immune modulation, biomimetic delivery, tumor microenvironment

INTRODUCTION

The advent of cancer immunotherapy has revolutionized oncological treatment paradigms by providing novel and effective strategies to combat a wide range of malignancies[1–4]. By leveraging the body's own immune system to recognize and eliminate cancer cells, immunotherapy offers a mechanism that is fundamentally distinct from traditional modalities such as chemotherapy and radiation[5–8]. Among the most impactful developments in this domain are immune checkpoint inhibitors (ICIs), which block proteins like PD-1/PD-L1 and CTLA-4 to restore T cell activity, and adoptive T cell therapies, including CAR-T cells, which are genetically engineered to target tumor-associated antigens[9, 10]. While these approaches have yielded durable responses and even curative outcomes in subsets of patients with cancers such as melanoma, lung cancer, and certain hematologic malignancies, they are not universally effective. Therapeutic resistance and low response rates in many solid tumors remain persistent clinical challenges[11].

A significant obstacle to broader immunotherapeutic success is the immunosuppressive nature of the tumor microenvironment (TME)[1, 12–14]. The TME comprises a complex network of stromal cells, extracellular matrix components, and immunoregulatory molecules that collectively contribute to immune evasion by tumors[15, 16]. This microenvironment can suppress antigen presentation, inhibit cytotoxic T lymphocyte (CTL) infiltration, and recruit immunosuppressive cells such as regulatory T cells (Tregs), myeloid-derived suppressor cells (MDSCs), and tumor-associated macrophages (TAMs). These features collectively hinder the immune system's ability to mount an effective anti-tumor response, thereby reducing the efficacy of ICIs and other immunotherapeutic agents. As such, new strategies aimed at remodeling or bypassing the TME to potentiate immune responses are of critical importance[17, 18].

One promising approach to overcome these limitations involves the use of innovative delivery systems capable of mimicking natural physiological mechanisms of intercellular communication[19, 20]. Exosomes, small

extracellular vesicles ranging from 30 to 150 nanometers in size, are naturally secreted by various cell types and are known to play a central role in cell-to-cell communication. In cancer, exosomes are implicated in antigen presentation, immune modulation, angiogenesis, and metastasis[21–24]. They carry bioactive molecules such as proteins, lipids, and nucleic acids, which can influence the behavior of recipient cells. In the context of immunotherapy, exosomes can potentially serve as carriers of tumor antigens or immune-activating molecules, making them attractive candidates for drug delivery and vaccine development.

However, despite their biological relevance, the clinical translation of native exosomes faces several technical and logistical challenges[25]. These include difficulties in large-scale production, batch-to-batch heterogeneity, rapid clearance from circulation, and limited targeting capability. To address these issues, researchers have developed exosome-mimetic nanoparticles (EMNs), engineered nanostructures designed to replicate the key functional attributes of natural exosomes while circumventing their limitations[25]. EMNs can be synthesized from either natural cell membranes or synthetic materials, and they retain crucial exosome-like properties such as biocompatibility, immune evasion, and target specificity. Moreover, EMNs offer enhanced design flexibility, making it possible to incorporate specific targeting ligands, immunostimulatory agents, or imaging probes, thereby expanding their utility in precision medicine[26].

The unique ability of EMNs to integrate biomimicry, immune modulation, and targeted delivery makes them highly suited for cancer immunotherapy applications. For example, EMNs derived from dendritic cell membranes can present tumor antigens to T cells, effectively functioning as nanovaccines[27]. Others can be loaded with checkpoint inhibitors, cytokines, or siRNAs to modulate the TME, reprogram immunosuppressive cells, or enhance T cell activation. Additionally, the ability of EMNs to home to tumor tissues via membrane-derived targeting features improves site-specific delivery and minimizes off-target effects[28–30].

Hence, exosome-mimetic nanoparticles represent a promising next-generation platform for enhancing cancer immunotherapy. By combining the natural advantages of exosomes with the versatility of nanotechnology, EMNs offer a novel strategy to overcome the limitations of current immunotherapeutic approaches. Ongoing research and clinical translation of EMNs hold great promise for expanding the reach and efficacy of immunotherapy across a broader spectrum of cancer types.

2. Exosomal Mimicry and Engineering Strategies

2. Design and Functionalization of Exosome-Mimetic Nanoparticles (EMNs)

Exosome-mimetic nanoparticles (EMNs) are emerging as promising alternatives to naturally secreted exosomes due to their scalable production and customizable features[31]. These nanoparticles are engineered to replicate the biological functions, structural properties, and targeting capabilities of natural exosomes, making them suitable platforms for therapeutic delivery and immune modulation. EMNs are primarily developed using two strategic approaches: top-down and bottom-up fabrication[32–34].

The top-down approach involves mechanical or chemical disruption of parental cells, followed by extrusion through filters or membranes of defined pore sizes. This process leads to the formation of membrane-derived vesicles that retain the membrane proteins, lipids, and surface markers of the source cells[35]. As a result, these EMNs exhibit biomimetic features that closely resemble natural exosomes, including membrane composition, antigen presentation machinery, and organotropism. This method has been successfully applied to generate EMNs from various immune cells such as dendritic cells, macrophages, and even tumor cells, leveraging their intrinsic signaling properties for targeted immunotherapy[36].

In contrast, the bottom-up approach allows the rational design of EMNs from synthetic components such as lipids, polymers, or hybrid materials[37]. These synthetic vesicles are often functionalized with exosomal proteins, peptides, or ligands that mimic the surface characteristics of exosomes. The advantage of this approach lies in the precise control it provides over the physicochemical parameters of the nanoparticles—such as size, surface charge, and payload composition—which can be tailored for specific applications. Moreover, bottom-up methods facilitate large-scale production and reproducibility, two critical considerations for clinical translation[37].

A hallmark of EMNs is their ability to preserve or incorporate key membrane proteins such as CD9, CD63, CD81 (tetraspanins), and major histocompatibility complex (MHC) molecules. These proteins are not only vital for maintaining structural stability and vesicle integrity but also play essential roles in immune recognition, cell adhesion, and antigen presentation[38]. By incorporating these molecules, EMNs can effectively engage immune cells, promote antigen-specific responses, and navigate through complex biological environments such as the tumor microenvironment (TME)[38].

To enhance targeting capabilities, EMNs can be engineered with functional ligands including antibodies, aptamers, or peptides that recognize tumor-associated antigens or immune receptors[39]. Furthermore, EMNs may be co-loaded or surface-decorated with immune stimulants such as CpG oligonucleotides, R848 (TLR7/8 agonist), or other adjuvants to promote dendritic cell maturation and T cell activation. These modifications enable EMNs to act as precision tools for personalized immunotherapy, especially when they are loaded with patient-specific tumor antigens or neoantigens[40].

Advanced bioengineering techniques such as click chemistry, electroporation, and lipid insertion have expanded the potential of EMNs as modular delivery systems. By incorporating nucleic acids (e.g., mRNA, siRNA),

immunogenic peptides, or cytokines (e.g., IL-2, GM-CSF), EMNs can be programmed to induce tailored immune responses[41]. Notably, hybrid EMNs that integrate synthetic cores with cell-derived membranes, particularly from dendritic cells or tumor cells, have demonstrated superior performance in antigen presentation and T cell priming, often outperforming their natural counterparts in preclinical models[41].

In sum, the design and functionalization of EMNs leverage the best of both biological mimicry and nanotechnological precision. Whether derived from top-down extrusion of immune cells or assembled de novo using bottom-up approaches, EMNs offer unmatched flexibility in their customization. Their ability to incorporate immunologically relevant proteins, respond to microenvironmental cues, and deliver a wide variety of therapeutic agents makes them potent candidates for next-generation cancer immunotherapies. As research advances, further optimization of EMN formulation and targeting strategies will be pivotal for their successful translation from bench to bedside.

3. Immune Modulation by Exosome-Mimetic Nanoparticles

One of the most compelling aspects of exosome-mimetic nanoparticles (EMNs) is their robust capacity to modulate the immune system[42]. Unlike conventional delivery systems, EMNs possess both intrinsic and engineered immunomodulatory properties, which they inherit from their parental cells or are endowed with through rational design. This enables them to engage various immune cell subsets within the tumor microenvironment (TME), shaping the overall immune landscape toward an anti-tumor state[42].

EMNs derived from antigen-presenting cells (APCs) such as dendritic cells and macrophages are especially potent in enhancing immunogenic responses[43]. These EMNs retain or mimic surface molecules like MHC class I and II, CD86, and ICAM-1, all of which are essential for antigen presentation and co-stimulatory signaling. By delivering antigens in the context of these surface markers, EMNs can promote cross-priming of cytotoxic T lymphocytes (CTLs) and facilitate their clonal expansion[44]. This process is critical for recognizing and eliminating tumor cells that express the corresponding antigens.

In addition to promoting T cell activation, EMNs can directly influence the behavior of innate immune cells. For instance, EMNs carrying toll-like receptor (TLR) agonists or pro-inflammatory cytokines can reprogram tumor-associated macrophages (TAMs) from an M2 (anti-inflammatory, pro-tumor) phenotype to an M1 (pro-inflammatory, anti-tumor) phenotype[45]. This reprogramming is associated with enhanced phagocytosis, cytokine production, and improved antigen presentation, thereby contributing to the breakdown of immune tolerance in the TME[45].

Engineered EMNs have also been used to deliver immunomodulatory molecules such as interleukin-12 (IL-12), granulocyte-macrophage colony-stimulating factor (GM-CSF), or small interfering RNAs (siRNAs) targeting immune checkpoint molecules like PD-L1[46]. By knocking down PD-L1 expression on tumor or immune cells, EMNs can relieve T cell exhaustion and restore cytotoxic activity. Similarly, EMNs delivering mRNA encoding costimulatory ligands can help amplify T cell responses and prevent immune escape mechanisms that tumors commonly exploit[46].

Importantly, the nano-size and lipid bilayer structure of EMNs facilitate their uptake by lymphoid organs and immune cells such as dendritic cells, B cells, and macrophages. Their size allows for efficient trafficking through lymphatic drainage pathways to lymph nodes, where antigen presentation and T cell priming are initiated[47]. Compared to free-floating proteins or drugs, EMNs exhibit improved stability, reduced degradation, and lower systemic toxicity, making them ideal vehicles for localized immune activation[47].

The tolerogenic or immunogenic profile of EMNs can also be fine-tuned depending on the therapeutic goal. For example, EMNs designed for autoimmune disease treatment can deliver tolerogenic signals or regulatory T cell (Treg)-inducing factors, while those for cancer therapy can deliver strong immunostimulatory cues[48]. This versatility offers a platform not just for oncology, but also for vaccines, allergy therapies, and transplantation immunology. Moreover, studies have shown that repeated administration of EMNs does not elicit strong adverse immune responses or toxicity, suggesting good biocompatibility and safety profiles. This positions EMNs favorably for long-term use in chronic conditions such as cancer or infectious diseases requiring booster immunizations[49].

Hence, EMNs hold significant promise as next-generation immunomodulators capable of reshaping the tumor immune microenvironment. By leveraging both passive biological mimicry and active engineering, EMNs can enhance antigen presentation, reverse immune suppression, and activate effector immune cells. Their capacity for targeted delivery and immune engagement places them at the forefront of modern immunotherapeutic strategies, especially when combined with existing modalities like immune checkpoint blockade or cancer vaccines.

4. EMNs as Delivery Vehicles in Cancer Immunotherapy

In the rapidly evolving landscape of cancer immunotherapy, efficient delivery of therapeutic agents to immune cells and tumor sites remains a formidable challenge. Factors such as rapid systemic clearance, poor tumor accumulation, off-target toxicity, and degradation of therapeutic payloads significantly limit treatment efficacy[32, 50]. Exosome-mimetic nanoparticles (EMNs), due to their structural and functional resemblance to natural exosomes, offer a highly effective platform for targeted and sustained delivery of immunotherapeutic agents.

EMNs possess a lipid bilayer that enables them to encapsulate a wide variety of therapeutic cargo, including proteins, peptides, small molecule drugs, and nucleic acids such as mRNA or siRNA[51]. This structural versatility allows EMNs to function as multimodal delivery vehicles, protecting sensitive payloads from degradation and facilitating their controlled release at the site of interest. Furthermore, their surface can be engineered with ligands, antibodies, or targeting moieties that recognize specific cell types or tumor markers, enhancing the precision of delivery[51].

One of the most promising uses of EMNs is the delivery of immune checkpoint inhibitors (ICIs), such as monoclonal antibodies targeting PD-1, PD-L1, or CTLA-4. Instead of systemic administration, which is often associated with immune-related adverse events, EMNs can deliver ICIs directly to the tumor or draining lymph nodes[52]. This targeted delivery strategy improves therapeutic efficacy while minimizing systemic toxicity. In some formulations, EMNs are co-loaded with ICIs and tumor antigens, thereby combining checkpoint blockade with antigen-specific T cell activation in a single platform[52].

EMNs also show great potential in cancer vaccine development. They can be loaded with tumor-associated antigens or patient-specific neoantigens and delivered to dendritic cells to promote antigen processing and presentation[53]. These EMNs stimulate the activation and proliferation of cytotoxic T lymphocytes that specifically recognize tumor cells, leading to a more robust and durable anti-tumor immune response. By mimicking the natural pathways of exosome trafficking, EMNs are more readily internalized by antigen-presenting cells compared to synthetic nanoparticles[53].

Moreover, EMNs can be engineered to respond to tumor-specific stimuli such as pH, redox gradients, or enzyme activity. This stimulus-responsive behavior ensures that cargo is preferentially released within the tumor microenvironment, further enhancing therapeutic specificity[54]. For example, EMNs can be designed to disassemble in acidic pH or release siRNA only in the presence of tumor-associated enzymes like matrix metalloproteinases.

For personalized immunotherapy, EMNs offer unparalleled flexibility. Tumor biopsies or patient-derived cells can be used to produce EMNs loaded with neoantigens unique to an individual's tumor. This approach enables the generation of customized cancer vaccines that elicit patient-specific immune responses. Furthermore, EMNs can be combined with adjuvants or cytokines such as IL-2, GM-CSF, or IFN-γ to amplify immune responses and counteract tumor-mediated immunosuppression[55]. Lastly, EMNs exhibit excellent pharmacokinetics and biodistribution. Their stability in circulation, reduced clearance by the mononuclear phagocyte system, and ability to penetrate tumor tissues contribute to improved therapeutic indices. Unlike synthetic nanocarriers, EMNs are inherently biocompatible and have shown minimal immunogenicity in preclinical studies, supporting their potential for clinical application[56, 57].

EMNs represent a new frontier in cancer immunotherapy by acting as intelligent, biocompatible delivery systems. Their ability to encapsulate and target a wide range of immunotherapeutic agents, coupled with their potential for personalization and immune modulation, makes them indispensable tools in the ongoing effort to develop more effective and safer cancer treatments. With continued innovation in their design and functionalization, EMNs are poised to redefine how immunotherapies are delivered and experienced by patients.

5. Challenges and Future Perspectives

Despite their promising preclinical performance, the clinical translation of EMNs faces several challenges. Manufacturing reproducibility, batch-to-batch consistency, and large-scale production remain critical hurdles. Standardized protocols for EMN isolation, characterization, and quality control are essential for regulatory approval and clinical success.

Another challenge is the potential for unwanted immune activation or off-target effects due to the presence of immunogenic epitopes or improper targeting. Long-term safety, biodistribution, and pharmacokinetics of EMNs must be thoroughly evaluated in vivo. Furthermore, strategies to optimize cargo loading, endosomal escape, and tissue-specific delivery are actively being explored to improve therapeutic outcomes.

Future research will likely focus on integrating EMNs with other therapeutic modalities such as CAR-T cells, radiotherapy, or chemotherapy to enhance synergistic responses. Additionally, the convergence of EMNs with artificial intelligence, systems biology, and microfluidic manufacturing could revolutionize their design and optimization for precision immunotherapy. With continued advances, EMNs are poised to play a transformative role in the next generation of cancer treatment.

CONCLUSION

Exosome-mimetic nanoparticles (EMNs) represent a cutting-edge advancement in cancer immunotherapy, combining the unique benefits of natural extracellular vesicles with the tunability and scalability of synthetic nanomaterials. These bioinspired platforms are engineered to mimic the size, structure, and surface functionality of native exosomes, allowing them to exploit endogenous cellular pathways for targeted delivery and immune system interaction. By bridging the gap between synthetic nanoparticles and biological vesicles, EMNs achieve improved biocompatibility, prolonged circulation time, and enhanced tumor targeting, while reducing off-target effects and systemic toxicity. Moreover, EMNs can be tailored to carry a wide array of therapeutic payloads, including tumor antigens, immunostimulatory agents, small molecule drugs, and RNA therapeutics, thereby enabling a multifaceted approach to cancer treatment. Their inherent immunomodulatory capacity makes them

particularly attractive for enhancing antigen presentation, activating cytotoxic T cells, and reversing tumor-induced immunosuppression. As research continues to optimize their composition—ranging from top-down approaches using cell membranes to bottom-up assembly using functionalized lipids or polymers—EMNs are increasingly being recognized as versatile and potent platforms for next-generation immunotherapies. Continued innovations in their design, large-scale manufacturing, and integration with other treatment modalities, such as immune checkpoint inhibitors and CAR-T cells, will be pivotal in realizing their clinical potential in oncology.

REFERENCES

1. 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. Mol. Cancer. 24, 160 (2025). https://doi.org/10.1186/s12943-025-02357-z
2. Gholami, A., Mohkam, M., Soleimanian, S., Sadraeian, M., Lauto, A.: Bacterial nanotechnology as a paradigm in targeted cancer therapeutic delivery and immunotherapy. Microsyst. Nanoeng. 10, 1–43 (2024). https://doi.org/10.1038/s41378-024-00743-z
3. Alum, E.U.: AI-driven biomarker discovery: enhancing precision in cancer diagnosis and prognosis. Discov. Oncol. 16, 313 (2025). https://doi.org/10.1007/s12672-025-02064-7
4. Jiang, Y., Wang, C., Zu, C., Rong, X., Yu, Q., Jiang, J.: Synergistic Potential of Nanomedicine in Prostate Cancer Immunotherapy: Breakthroughs and Prospects. Int. J. Nanomedicine. 19, 9459–9486 (2024). https://doi.org/10.2147/IJN.S466396
5. Anand, U., Dey, A., Chandel, A.K.S., Sanyal, R., Mishra, A., Pandey, D.K., De Falco, V., Upadhyay, A., Kandimalla, R., Chaudhary, A., Dhanjal, J.K., Dewanjee, S., Vallamkondu, J., Pérez de la Lastra, J.M.: Cancer chemotherapy and beyond: Current status, drug candidates, associated risks and progress in targeted therapeutics. Genes Dis. 10, 1367–1401 (2022). https://doi.org/10.1016/j.gendis.2022.02.007
6. Cao, L., Zhu, Y., Wang, W., Wang, G., Zhang, S., Cheng, H.: Emerging Nano-Based Strategies Against Drug Resistance in Tumor Chemotherapy. Front. Bioeng. Biotechnol. 9, (2021). https://doi.org/10.3389/fbioe.2021.798882
7. Ghattass, K., Assah, R., El-Sabban, M., Gali-Muhtasib, H.: Targeting Hypoxia for Sensitization of Tumors to Radio- and Chemotherapy. Curr. Cancer Drug Targets. 13, 670–685 (2013). https://doi.org/10.2174/15680096113139990004
8. Aja, P.M., Agu, P.C., Musyoka, A.M., Ngwueche, W., Odo, J.U., Fasogbon, I.V., Herbert, M., Daniel Eze, E.: Integrative Approaches to Prostate Disease Management: Nutrition, Exercise, and Lifestyle Modifications. Am. J. Mens Health. 19, 15579883251344571 (2025). https://doi.org/10.1177/15579883251344571
9. Tufail, T., Uti, D.E., Aja, P.M., Offor, C.E., Ibiam, U.A., Ukaidi, C.U.A.: Utilizing Indigenous Flora in East Africa for Breast Cancer Treatment: An Overview. Anticancer Agents Med. Chem. 25, 99–113 (2025). https://doi.org/10.2174/0118715206338557240909081833
10. 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
11. Dagar, G., Gupta, A., Masoodi, T., Nisar, S., Merhi, M., Hashem, S., Chauhan, R., Dagar, M., Mirza, S., Bagga, P., Kumar, R., Akil, A.S.A.-S., Macha, M.A., Haris, M., Uddin, S., Singh, M., Bhat, A.A.: Harnessing the potential of CAR-T cell therapy: progress, challenges, and future directions in hematological and solid tumor treatments. J. Transl. Med. 21, 449 (2023). https://doi.org/10.1186/s12967-023-04292-3
12. Chen, B., Dai, W., He, B., Zhang, H., Wang, X., Wang, Y., Zhang, Q.: Current Multistage Drug Delivery Systems Based on the Tumor Microenvironment. Theranostics. 7, 538–558 (2017). https://doi.org/10.7150/thno.16684
13. Alum, E.U., Uti, D.E., Ugwu, O.P.-C., Alum, B.N., Edeh, F.O., Ainebyoona, C.: Unveiling the microbial orchestra: exploring the role of microbiota in cancer development and treatment. Discov. Oncol. 16, 646 (2025). https://doi.org/10.1007/s12672-025-02352-2
14. Emami Nejad, A., Najafgholian, S., Rostami, A., Sistani, A., Shojaeifar, S., Esparvarinha, M., Nedaeinia, R., Haghjooy Javanmard, S., Taherian, M., Ahmadlou, M., Salehi, R., Sadeghi, B., Manian, M.: The role of hypoxia in the tumor microenvironment and development of cancer stem cell: a novel approach to developing treatment. Cancer Cell Int. 21, 62 (2021). https://doi.org/10.1186/s12935-020-01719-5
15. 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
16. Khalaf, K., Hana, D., Chou, J.T.-T., Singh, C., Mackiewicz, A., Kaczmarek, M.: Aspects of the Tumor Microenvironment Involved in Immune Resistance and Drug Resistance. Front. Immunol. 12, 656364 (2021). https://doi.org/10.3389/fimmu.2021.656364

17. 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
18. Tie, Y., Tang, F., Wei, Y., Wei, X.: Immunosuppressive cells in cancer: mechanisms and potential therapeutic targets. J. Hematol. Oncol.J Hematol Oncol. 15, 61 (2022). https://doi.org/10.1186/s13045-022-01282-8
19. Ezike, T.C., Okpala, U.S., Onoja, U.L., Nwike, C.P., Ezeako, E.C., Okpara, O.J., Okoroafor, C.C., Eze, S.C., Kalu, O.L., Odoh, E.C., Nwadike, U.G., Ogbodo, J.O., Umeh, B.U., Ossai, E.C., Nwanguma, B.C.: Advances in drug delivery systems, challenges and future directions. Heliyon. 9, e17488 (2023). https://doi.org/10.1016/j.heliyon.2023.e17488
20. Sun, B., Li, R., Ji, N., Liu, H., Wang, H., Chen, C., Bai, L., Su, J., Chen, J.: Brain-targeting drug delivery systems: The state of the art in treatment of glioblastoma. Mater. Today Bio. 30, 101443 (2025). https://doi.org/10.1016/j.mtbio.2025.101443
21. Araujo-Abad, S., Berna, J.M., Lloret-Lopez, E., López-Cortés, A., Saceda, M., de Juan Romero, C.: Exosomes: from basic research to clinical diagnostic and therapeutic applications in cancer. Cell. Oncol. 48, 269–293 (2025). https://doi.org/10.1007/s13402-024-00990-2
22. Choi, H., Choi, Y., Yim, H.Y., Mirzaaghasi, A., Yoo, J.-K., Choi, C.: Biodistribution of Exosomes and Engineering Strategies for Targeted Delivery of Therapeutic Exosomes. Tissue Eng. Regen. Med. 18, 499–511 (2021). https://doi.org/10.1007/s13770-021-00361-0
23. Akwari, A.Ak., Okoroh, P.N., Aniokete, U.C., Abba, J.N.: 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
24. Fawzy, M.P., Hassan, H.A.F.M., Amin, M.U., Preis, E., Bakowsky, U., Fahmy, S.A.: Deploying nucleic acids-loaded plant-derived exosomes as green nano gadget in cancer gene therapy. Mater. Adv. 6, 1230–1261 (2025). https://doi.org/10.1039/D4MA01189A
25. Rezaie, J., Feghhi, M., Etemadi, T.: A review on exosomes application in clinical trials: perspective, questions, and challenges. Cell Commun. Signal. 20, 145 (2022). https://doi.org/10.1186/s12964-022-00959-4
26. Song, J., Song, B., Yuan, L., Yang, G.: Multiplexed strategies toward clinical translation of extracellular vesicles. Theranostics. 12, 6740–6761 (2022). https://doi.org/10.7150/thno.75899
27. Liu, H., Lu, Y., Zong, J., Zhang, B., Li, X., Qi, H., Yu, T., Li, Y.: Engineering dendritic cell biomimetic membrane as a delivery system for tumor targeted therapy. J. Nanobiotechnology. 22, 663 (2024). https://doi.org/10.1186/s12951-024-02913-7
28. Eskandari-Malayeri, F., Rezaei, M.: Immune checkpoint inhibitors as mediators for immunosuppression by cancer-associated fibroblasts: A comprehensive review. Front. Immunol. 13, 996145 (2022). https://doi.org/10.3389/fimmu.2022.996145
29. 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. Discov. Nano. 20, 70 (2025). https://doi.org/10.1186/s11671-025-04248-0
30. 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. J. Nanobiotechnology. 23, 336 (2025). https://doi.org/10.1186/s12951-025-03412-z
31. Chen, H., Li, Q.: Recent advances in scalable exosome production: Challenges and innovations. Chin. J. Plast. Reconstr. Surg. (2025). https://doi.org/10.1016/j.cjprs.2025.05.001
32. Rana, R., Devi, S.N., Bhardwaj, A.K., Yashavarddhan, M.H., Bohra, D., Ganguly, N.K.: Exosomes as nature's nano carriers: Promising drug delivery tools and targeted therapy for glioma. Biomed. Pharmacother. 182, 117754 (2025). https://doi.org/10.1016/j.biopha.2024.117754
33. Premchandani, T., Tatode, A., Taksande, J., Umekar, M., Qutub, M., Hussain, U.M., Singanwad, P.: Engineered Exosomes as Smart Drug Carriers: Overcoming Biological Barriers in CNS and Cancer Therapy. Drugs Drug Candidates. 4, 19 (2025). https://doi.org/10.3390/ddc4020019
34. Parada, N., Romero-Trujillo, A., Georges, N., Alcayaga-Miranda, F.: Camouflage strategies for therapeutic exosomes evasion from phagocytosis. J. Adv. Res. 31, 61–74 (2021). https://doi.org/10.1016/j.jare.2021.01.001
35. Li, Y.-J., Wu, J.-Y., Liu, J., Xu, W., Qiu, X., Huang, S., Hu, X.-B., Xiang, D.-X.: Artificial exosomes for translational nanomedicine. J. Nanobiotechnology. 19, 242 (2021). https://doi.org/10.1186/s12951-021-00986-2
36. Xu, X., Xu, L., Wen, C., Xia, J., Zhang, Y., Liang, Y.: Programming assembly of biomimetic exosomes: An emerging theranostic nanomedicine platform. Mater. Today Bio. 22, 100760 (2023). https://doi.org/10.1016/j.mtbio.2023.100760

37. Donghia, D., Baldassari, S., Drava, G., Ailuno, G., Caviglioli, G.: Insights on Natural Membrane Characterization for the Rational Design of Biomimetic Drug Delivery Systems. Pharmaceutics. 17, 841 (2025). https://doi.org/10.3390/pharmaceutics17070841
38. Jankovičová, J., Sečová, P., Michalková, K., Antalíková, J.: Tetraspanins, More than Markers of Extracellular Vesicles in Reproduction. Int. J. Mol. Sci. 21, 7568 (2020). https://doi.org/10.3390/ijms21207568
39. Bajracharya, R., Song, J.G., Patil, B.R., Lee, S.H., Noh, H.-M., Kim, D.-H., Kim, G.-L., Seo, S.-H., Park, J.-W., Jeong, S.H., Lee, C.H., Han, H.-K.: Functional ligands for improving anticancer drug therapy: current status and applications to drug delivery systems. Drug Deliv. 29, 1959–1970. https://doi.org/10.1080/10717544.2022.2089296
40. Sidoti Migliore, G., Pezzino, G., Cavaliere, R., De Pasquale, C., Ferlazzo, G.: On immunostimulants and dendritic cell activation. Immunol. Lett. 232, 45–47 (2021). https://doi.org/10.1016/j.imlet.2021.02.004
41. Amoako, K., Mokhammad, A., Malik, A., Yesudasan, S., Wheba, A., Olagunju, O., Gu, S.X., Yarovinsky, T., Faustino, E.V.S., Nguyen, J., Hwa, J.: Enhancing nucleic acid delivery by the integration of artificial intelligence into lipid nanoparticle formulation. Front. Med. Technol. 7, 1591119 (2025). https://doi.org/10.3389/fmedt.2025.1591119
42. Li, J., Wang, J., Chen, Z.: Emerging role of exosomes in cancer therapy: progress and challenges. Mol. Cancer. 24, 13 (2025). https://doi.org/10.1186/s12943-024-02215-4
43. Shenoda, B.B., Ajit, S.K.: Modulation of Immune Responses by Exosomes Derived from Antigen-Presenting Cells. Clin. Med. Insights Pathol. 9, 1–8 (2016). https://doi.org/10.4137/CPath.S39925
44. Muntjewerff, E.M., Meesters, L.D., van den Bogaart, G.: Antigen Cross-Presentation by Macrophages. Front. Immunol. 11, (2020). https://doi.org/10.3389/fimmu.2020.01276
45. Zheng, R., Ma, J.: Immunotherapeutic Implications of Toll-like Receptors Activation in Tumor Microenvironment. Pharmaceutics. 14, 2285 (2022). https://doi.org/10.3390/pharmaceutics14112285
46. Kang, S., Mansurov, A., Kurtanich, T., Chun, H.R., Slezak, A.J., Volpatti, L.R., Chang, K., Wang, T., Alpar, A.T., Refvik, K.C., Hansen, O.I., Borjas, G.J., Berg, B.T.K., Shim, H.-N., Hultgren, K.T., Gomes, S., Wang, Y., Solanki, A., Ishihara, J., Swartz, M.A., Hubbell, J.A.: Engineered GM-CSF polarizes protumorigenic tumor-associated macrophages to an antitumorigenic phenotype and potently synergizes with IL-12 immunotherapy. J. Immunother. Cancer. 12, e009541 (2024). https://doi.org/10.1136/jitc-2024-009541
47. 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. Biomed. Pharmacother. 167, 115597 (2023). https://doi.org/10.1016/j.biopha.2023.115597
48. Xiang, Y., Zhang, M., Jiang, D., Su, Q., Shi, J.: The role of inflammation in autoimmune disease: a therapeutic target. Front. Immunol. 14, 1267091 (2023). https://doi.org/10.3389/fimmu.2023.1267091
49. Moorman, C.D., Sohn, S.J., Phee, H.: Emerging Therapeutics for Immune Tolerance: Tolerogenic Vaccines, T cell Therapy, and IL-2 Therapy. Front. Immunol. 12, 657768 (2021). https://doi.org/10.3389/fimmu.2021.657768
50. Dara, M., Dianatpour, M., Azarpira, N., Tanideh, N., Tanideh, R.: Integrating CRISPR technology with exosomes: Revolutionizing gene delivery systems. Biochem. Biophys. Res. Commun. 740, 151002 (2024). https://doi.org/10.1016/j.bbrc.2024.151002
51. Shtykalova, S., Deviatkin, D., Freund, S., Egorova, A., Kiselev, A.: Non-Viral Carriers for Nucleic Acids Delivery: Fundamentals and Current Applications. Life. 13, 903 (2023). https://doi.org/10.3390/life13040903
52. Wojtukiewicz, M.Z., Rek, M.M., Karpowicz, K., Górska, M., Polityńska, B., Wojtukiewicz, A.M., Moniuszko, M., Radziwon, P., Tucker, S.C., Honn, K.V.: Inhibitors of immune checkpoints—PD-1, PD-L1, CTLA-4—new opportunities for cancer patients and a new challenge for internists and general practitioners. Cancer Metastasis Rev. 40, 949–982 (2021). https://doi.org/10.1007/s10555-021-09976-0
53. Pan, R.-Y., Chung, W.-H., Chu, M.-T., Chen, S.-J., Chen, H.-C., Zheng, L., Hung, S.-I.: Recent Development and Clinical Application of Cancer Vaccine: Targeting Neoantigens. J. Immunol. Res. 2018, 4325874 (2018). https://doi.org/10.1155/2018/4325874
54. Thomas, R.G., Surendran, S.P., Jeong, Y.Y.: Tumor Microenvironment-Stimuli Responsive Nanoparticles for Anticancer Therapy. Front. Mol. Biosci. 7, (2020). https://doi.org/10.3389/fmolb.2020.610533
55. Singh, P., Khatib, M.N., R, R., Kaur, M., Srivastava, M., Barwal, A., Rajput, G.V.S., Rajput, P., Syed, R., Sharma, G., Kumar, S., Shabil, M., Pandey, S., Brar, M., Bushi, G., Mehta, R., Sah, S., Goh, K.W., Satapathy, P., Gaidhane, A.M., Samal, S.K.: Advancements and challenges in personalized neoantigen-based cancer vaccines. Oncol. Rev. 19, 1541326 (2025). https://doi.org/10.3389/or.2025.1541326
56. 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

57. Li, J., Wang, J., Chen, Z.: Emerging role of exosomes in cancer therapy: progress and challenges. Mol. Cancer. 24, 13 (2025). https://doi.org/10.1186/s12943-024-02215-4

CITE AS: Mpora Kakwanzi Evelyn (2025). Exosome-Mimetic Nanoparticles in Cancer Immunotherapy: Mimicry, Modulation, and Delivery. NEWPORT INTERNATIONAL JOURNAL OF SCIENTIFIC AND EXPERIMENTAL SCIENCES 6(3):62-69 https://doi.org/10.59298/NIJSES/2025/63.6269