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Immune-modulatory biomimetic nanoparticles: Advances in design, mechanisms, and nanomedicine applications

Somayeh Vandghanooni[1*], Parniya Kehtari[2], Niloufar Ahdeno[2]

[1]Hematology and Oncology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
[2]Research Center for Pharmaceutical Nanotechnology, Biomedicine Institute, Tabriz University of Medical Sciences, Tabriz, Iran

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Abstract

The development of biomimetic nanoparticles (NPs) represents an innovative approach to address the lacks of conventional drug delivery systems. This advancement demonstrates promising potential in immunotherapy. Biomimetic NPs imitate biological structures to improve the effectiveness of drug delivery and enhance interactions with cancer cells. Their beneficial features include biocompatibility, long circulation time, tissue specificity, enhanced drug absorption, and low toxicity. Recent advancements confirm the efficacy of biomimetic NPs especially cell-membrane coated biomimetic NPs in immune modulation in cancer and inflammatory diseases. Furthermore, their integration with innovative gene engineering techniques, such as mRNA therapeutics and CRISPR-Cas9, for immune system targeting represents a novel therapeutic approach. This editorial explains the potential of biomimetic NPs in tumor immunotherapy and precision medicine, as well as the challenges they face in clinical translation, including biodistribution, long-term biosafety, the risk of unexpected activation of the immune system and scalability. Future recommendations emphasize the use of advanced biosensing tracking systems and the standardization of production for medicinal translation. BioImpacts invites researchers and scholars involved in this interdisciplinary field to collaborate to advance innovation at the intersection of nanotechnology and immunology.

Keywords: Biomimetic nanoparticles, Immunotherapy, Immune modulation, Nanomedicine, Cell membrane-coated nanoparticles, Precision medicine, mRNA therapeutics, CRISPR-Cas9

Biomimetic nanoparticles (NPs) represent a developing category of NPs that are coated with biomaterials, allowing them to mimic the biological characteristics and functions of natural cells. These NPs show significantly enhanced biocompatibility, high target specificity, extended retention time, and reduced unwanted immune responses. There are several types of biomaterials/systems that can be employed to fabricate the biomimetic NPs. These include cell membranes derived from macrophages and dendritic cells, as well as exosomes, which facilitate precise interactions with disease microenvironments.[1] These NPs surpass the restrictions of conventional drug delivery systems, offering designs inspired by nature for active modulation of immune response.[2-4] One of the main function of these NPs is to reprogram immune responses through different mechanisms. For example, their action in transforming immunosuppressive M2 macrophages into tumor-fighting M1 phenotypes in triple-negative breast cancer[5] or enhancing T-cell activity in glioblastoma through cancer cell membrane-coated biomimetic NPs has been proven.[6] Surface modification of biomimetic NPs improves specific affinity and immunomodulation, which enhances therapeutic efficacy in tumor immunotherapy.

In 2025, strong preclinical results in biomimetic therapeutic strategies are now entering early-stage clinical trials. Notable examples include the Phase I trial NCT03608631, which continues as a single center at MD Anderson Cancer Center until late 2025. This trial investigates the efficacy of mesenchymal stromal cell-derived exosome NPs loaded with KrasG12D siRNA for metastatic pancreatic cancer. Findings demonstrated early acceptability and tumor-specific gene silencing in patient.[7] Another study (completed Phase I NCT01294072, multicenter across the United States) evaluated plant-derived exosomal NPs containing curcumin for oral drug delivery in advanced colorectal cancer. Results demonstrated increased bioavailability and minimal side effects, inspiring subsequent Phase II designs.[8] Collectively, these fundamental studies, demonstrate the development of biomimetic NPs toward mainstream therapeutic integration and hold promise for

*Corresponding author: Somayeh Vandghanooni, Email: vandghanoonis@tbzmed.ac.ir

personalized and low-toxicity interventions.

The new advancement in the development of biomimetic NPs demonstrates their versatile potential in immunotherapy.[9,10] In this context, developing studies disclose novel mechanisms and improved effectiveness of biomimetic NPs in various diseases. Hybrid biomimetic NPs incorporated with immune checkpoint inhibitors are an effective therapeutic strategy for resistant cancers through remodeling of tumor microenvironment (TME).[11,12] A recent publication reported hybrid NPs-immune cell conjugates (NCCs) as an effective immunotherapeutic enhancer that directly interacts with immune cells, enhancing checkpoint blockade competence and overwhelming resistance in solid tumors.[13] Hybrid biomimetic NPs targeting regulatory T cells in combination with checkpoint inhibitors, such as anti-PD-1/PD-L1, have demonstrated considerable tumor growth inhibition in resistant tumor models by inhibiting immunosuppressive cells and improving effector T cell infiltration.[14,15] Additionally, exosome-based biomimetic NPs are considered a suitable carrier for delivering anti-inflammatory cargos for autoimmune diseases, particularly rheumatoid arthritis (RA), to organize immune responses.[16] A new study showed the anti-inflammatory ability of developed M2-type macrophage-derived exosome NPs in RA models through macrophage polarization and cytokine modulation, which leads to suppression of joint inflammation.[17] Mesenchymal stem cells membrane-derived biomimetic NPs showed remarkable progress in targeted delivery of therapeutic payloads, which led to significant therapeutic outcomes.[18,19] Furthermore, the therapeutic potential of biomimetic NPs has been shown in 2024 research through miRNA delivery and immune tolerance induction.[20-22]

In gene-editing integrated systems, biomimetic NPs are being incorporated with genetic engineering techniques like CRISPR-Cas9 and mRNA therapeutics. This approach is advancing precision immunotherapy by enabling targeted inhibition of immunosuppressive pathways. MRNA therapeutics can induce robust immune response against tumor cells through production of specific proteins, while CRISPR technology can modify target genes associated with strong immune response and cancer progression.[23,24] The delivery of these systems using biomimetic NPs enhances the specificity and therapeutic index as well as reduces the off-target effects and diminishes the immunosuppressive properties of TME. Importantly, this approach could initiate new horizons toward personalized therapy according to the exclusive genetic profile of individual patients. The delivery of CRISPR/Cas9 using biomimetic NPs has the potential to enhance targeting accuracy and minimize off-target effects of genetic materials. In a new finding, triterpenoids-templated self-assembly biomimetic-based nanosystems have been applied for the delivery of CRISPR/Cas9 to edit genes in tumor cells for enhancing immune responses.[25] These cutting-edge developments, along with nanotechnology, immunology, and molecular therapeutics, introduce biomimetic NPs as a central focus in next-generation immunotherapies. Cell membrane-derived biomimetic NPs are considered as a potential carrier to avoid immune clearance and permit homologous targeting to enhance therapeutic efficacy.[26] As clinical application accelerates, these NPs promise broader impacts, from overcoming therapeutic resistance to personalized treatments for complex immune disorders.

Implementing the appropriate type of immune intervention, tailored to the immune activation status and administered at the optimal time, is crucial for effective precision immunotherapy. Biomimetic NPs are regarded as leading candidates in precision medicine, where the immune profiles of patients play a crucial role in the bioengineering of delivery systems, such as patient-derived cell membrane coatings.[27] In a recent study, surgically harvested cancer tissues were utilized to prepare personalized cancer cell membranes (CCMs) as tumor-associated antigens. The study focused on polymeric NPs encapsulating imiquimod (R837), which were coated with these personalized CCMs. The in vivo results demonstrated the effective migration of the NPs to the draining lymph nodes, where they were presented by plasmacytoid dendritic cells. This process elicited enhanced antitumor immune responses.[28]

From a societal perspective, biomimetic NPs hold promise for the globalization of advanced therapies. These NPs, when combined with genetic modification platforms such as mRNA-based vaccines or gene engineering systems, have the potential to reduce the cost and complexity of treatments such as CAR-T cell therapy. However, to achieve an efficient outcome, transitional challenges such as regulatory standardization and large-scale production must be overcome. In this regard, clinical-grade production of biotechnology-inspired designs, such as NPs coated with patient-derived cell membranes and their scalability, should be considered. In precision medicine, developing one-size-fits-all solutions is challengeable issue due to the patient heterogeneity. Also, determination of valid biomarker for patient selection remains a critical hurdle. Additionally, creating effective criteria to screen suitable patients for biomimetic-based therapy is necessary to optimize treatment outcomes. Additionally, navigating the regulatory landscape for new therapies can be complex due to differing requirements across regions. Also, the risk of unexpected activation of the immune system, especially in autoimmune diseases, must be assessed to ensure long-term safety. Further, to ensure a comprehensive understanding of the long-term safety profiles of these innovative NPs, it is essential to consider tissue distribution issues, including organ accumulation and elimination pathways, potential chronic effects, and

the risk of carcinogenicity. The long term studies will facilitate the safe integration of biomimetic NPs into the clinical applications and enhance therapeutic index. Also, addressing the chronic exposure and potential delayed effects are important for approval processes and public trust.[29] Continued research and interdisciplinary collaboration are necessary to transition biomimetic NPs from bench to bed to improve global health outcomes.

Conclusion and feature perspective

This editorial discusses the potential of biomimetic NPs in modulating the immune responses and advancing therapeutic strategies while addressing serious translational challenges. Recent developments highlight the significant effectiveness of biomimetic NPs, in modulating immune responses in cancer and inflammatory diseases. Moreover, their combination with cutting-edge gene engineering technologies, such as mRNA therapeutics and CRISPR-Cas9, for targeted immune system interventions introduces a revolutionary therapeutic strategy. Biomimetic NPs are emerging as key players in the field of precision medicine, leveraging individual profiles to design advanced drug delivery systems, including coatings derived from patient-specific cell membranes.

Even with the potential of biomimetic NPs in modulating immunosuppressive TME, some delivery challenges remain. Proper biodistribution with reduced off-target effects is the first complication in translational medicine. The development of biosensor systems for real-time tracking of biomimetic NPs is essential to follow unexpected accumulation in non-specific tissues. Moreover, to provide sustainable therapeutic outcomes in chronic diseases such as cancer, the long-term effect of biomimetic carriers on immune modulation must be evaluated. Precise silencing of immunosuppressive genes can be achieved through emerging gene editing platforms such as CRISPR-Cas9 or mRNA therapeutics in combination with biomimetic NPs. Optimized protocols must be established for scalable genetic engineering that facilitate clinical application. Overall, to best respond to these challenges, interdisciplinary experiments should be conducted to link immunology, nanotechnology, and clinical sciences together as a changing force in precision immunotherapy.

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Authors' Contribution

Conceptualization: Somayeh Vandghanooni.
Investigation: Somayeh Vandghanooni.
Resources: Somayeh Vandghanooni.
Supervision: Somayeh Vandghanooni.
Validation: Somayeh Vandghanooni.

Study Highlights

What is the current knowledge?

- Biomimetic NPs mimic natural component to improve biocompatibility, circulation time, and tissue targeting.
- Improved T-cell activity through checkpoint inhibitors and tumor microenvironment remodeling are main function of biomimetic NPs for tumor immunotherapy.
- Integration of biomimetic NPs with CRISPR-Cas9 and mRNA therapeutics enables precise gene editing and immune modulation.
- Patient-derived membrane coatings reduce off-target effects and support personalized immunotherapy.
- Key challenges include biodistribution control, production scalability, and long-term safety.

What is new here?

- Triterpenoids-templated biomimetic systems have been developed to deliver CRISPR-Cas9 to edit tumor genes and boost immunity.
- Precision immunotherapy is now adapting to the patient's immune status in real time using biomimetic platforms.
- Incorporation of biomimetic systems with mRNA platforms enhance the effectiveness of cell-based therapies.
- Advanced biosensors enable tracking of the behavior and distribution of NPs in vivo and in real-time.
- Standard clinical-level production protocols have been proposed to accelerate translational applications.

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Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability Statement

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The authors used ChatGPT-5 for editing and paraphrasing of different sections of the paper. The authors reviewed the text for accuracy and take full responsibility for the final content.

Ethical Approval

All data, findings, and interpretations presented in this article are based on previous rigorous scientific research, and no new data have been reported. We have accurately represented this information and made every effort to avoid misrepresentation or fabrication, ensuring that our presentation is clear and honest.

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