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Editorial

Nano-encapsulated CRISPR-based genome: Next-generation strategies to optimize delivery

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To Editor,

The advent of CRISPR-based genome editing has revolutionized molecular biology, offering unparalleled precision in manipulating genetic material. This transformative technology has paved the way for breakthroughs in medicine, agriculture, and biotechnology. However, the full potential of CRISPR remains constrained by a critical bottleneck: effective delivery of its components to target cells. Challenges such as off-target effects, immunogenicity, and limited tissue specificity continue to impede its translation from bench to bedside.[1] To overcome these hurdles, researchers are now exploring nano-encapsulation as a next-generation strategy to optimize CRISPR delivery.[2] CRISPR delivery traditionally relies on viral vectors, chemical transfection (lipofection), and physical methods like electroporation/nucleofection and microinjection.[3] While viral vectors are highly efficient, their use is limited by immunogenicity, size constraints, and the risk of insertional mutagenesis. Lipofection uses cationic lipid reagents to deliver CRISPR components into cells, though safer, often suffer from instability in circulation and suboptimal delivery efficiency to specific tissues. Physical methods, while precise, are largely impractical for systemic applications as well as high cell death may result from high voltage pulses. These limitations necessitate innovative solutions that combine precision, safety, and efficiency. Nano-encapsulation offers a promising alternative, leveraging the unique properties of nanomaterials to address the shortcomings of conventional delivery platforms.

Nano-encapsulation involves packaging CRISPR-Cas components within nanoscale carriers, such as lipid-based nanoparticles, polymeric particles, or exosomes. These carriers offer several advantages over traditional methods. They protect the CRISPR components from enzymatic degradation in the bloodstream, prolonging their half-life and enhancing their bioavailability. Additionally, nano-encapsulation allows for the functionalization of nano-carriers with targeting ligands, enabling precise delivery to specific cells or tissues. This is particularly critical for therapeutic applications, where unintended gene edits in non-target tissues can lead to adverse effects. Moreover,

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many nano-carriers are biocompatible and exhibit low immunogenicity, reducing the risk of systemic immune responses.[4] Recent advances in nanotechnology have further expanded the capabilities of nano-encapsulation for CRISPR delivery. Multifunctional nano-carriers are being developed, integrating targeting moieties, imaging agents, and stimuli-responsive release mechanisms. For example, pH-sensitive nano-carriers can release CRISPR components in the acidic environment of endosomes, ensuring efficient intracellular delivery.[5] Similarly, magnetic nanoparticles can be guided to target tissues using external magnetic fields, enhancing precision. These innovations have shown promising results in preclinical studies, with some systems demonstrating effective gene editing in vivo with minimal off-target effects. The therapeutic applications of nano-encapsulated CRISPR are vast and varied. In genetic disorders, this approach could enable the correction of disease-causing mutations with unprecedented accuracy. Cancer therapy is another promising avenue, where CRISPR can be used to target oncogenic pathways or enhance the efficacy of immunotherapy. Infectious diseases, too, stand to benefit, as CRISPR can be harnessed to disrupt viral genomes or modulate host immune responses.[6] Beyond these, nano-encapsulation opens new possibilities for personalized medicine, allowing genome editing to be tailored to individual patients and specific disease contexts.[7] Despite its immense potential, nano-encapsulation for CRISPR delivery is not without challenges. The scalability of nano-carrier production and the reproducibility of their performance in clinical settings remain significant barriers.[8,9] Furthermore, the complexity of nano-carrier systems necessitates rigorous testing to ensure their safety and efficacy. Ethical considerations also play a crucial role, as the precision of CRISPR delivery must be balanced against the risk of unintended consequences, particularly in germline editing.[10] Robust regulatory frameworks will be essential to navigate these issues and build public trust in this emerging technology. Looking ahead, the integration of nano-encapsulation with CRISPR represents a paradigm shift in genome editing. By addressing the delivery challenges that have long hindered clinical translation of CRISPR, this approach could unlock new frontiers in gene therapy and regenerative medicine. Realizing this vision will require interdisciplinary collaboration, bringing together experts in nanotechnology, molecular biology, and clinical medicine. Continued investment in research and innovation will be critical to refining nano-encapsulation strategies and scaling them for widespread clinical use.

In conclusion, the fusion of CRISPR technology with nanotechnology heralds a new era in genome editing. Nano-encapsulation offers a versatile and efficient platform for overcoming the longstanding challenges of CRISPR delivery, bringing us closer to the dream of precise, safe, and effective gene editing. As we stand on the cusp of this breakthrough, it is imperative to address the remaining hurdles through dedicated research and collaboration. The future of CRISPR-based therapies depends not only on the power of the editing tools themselves but also on our ability to deliver them where they are needed most.

Conflict of Interest

None.

References

1. Chen M, Mao A, Xu M, Weng Q, Mao J, Ji J. CRISPR-Cas9 for cancer therapy: Opportunities and challenges. *Cancer lett*. 2019;447:48–55.
2. Chen C, Zhong W, Du S, Li Y, Zeng Y, Liu K. Intelligent nanotherapeutic strategies for the delivery of CRISPR system. *Acta Pharm Sinica B*. 2023;13(6):2510–53.
3. Lino CA, Harper JC, Carney JP, Timlin JA. Delivering CRISPR: a review of the challenges and approaches. *Drug Deliv*. 2018;25(1):1234–57.
4. Wang Z, Wang X, Xu W, Li Y, Lai R, Qiu X. Translational Challenges and Prospective Solutions in the Implementation of Biomimetic Delivery Systems. *Pharmaceutics*. 2023;15(11):2623.
5. Naeem M, Hoque MZ, Ovais M, Basheer C, Ahmad I. Stimulus-Responsive Smart Nanoparticles-Based CRISPR-Cas Delivery for Therapeutic Genome Editing. *Int J Mol Sci*. 2021;22(20):11300.
6. Badia R, Garcia-Vidal E, Ballana E. Viral-Host Dependency Factors as Therapeutic Targets to Overcome Antiviral Drug-Resistance: A Focus on Innate Immune Modulation. *Front Virol*. 2022;2:1–17.
7. Dinh L, Mahon L, Yan B. Nano-Encapsulation and Conjugation Applied in the Development of Lipid Nanoparticles Delivering Nucleic Acid Materials to Enable Gene Therapies. *Appl Nano*. 2024;5(3):143–61.
8. Pandey T, Pandey V. Microbial assistance in nano-carrier development: Innovative strategies in drug delivery. *J Drug Deliv Sci Technol*. 2024;95:105607.
9. Ebrahimi N, Manavi MS, Nazari A, Momayezi A, Faghihkhorasani F, Abdulwahid RR. Nano-scale delivery systems for siRNA delivery in cancer therapy: New era of gene therapy empowered by nanotechnology. *Environ Res*. 2023;239(2):117263.
10. Aljabali A, El-Tanani M, Tambuwala MM. Principles of CRISPR-Cas9 technology: Advancements in genome editing and emerging trends in drug delivery. *J Drug Deliv Sci Technol*. 2024;92:105338.

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