IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 2, December 2025
Impact Factor: 7.67

Gene Delivery System: Novel Approaches for Nucleic Acid Therapeutics

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Abstract: *There is growing need for a safe, efficient, specific and non-pathogenic means for delivery of gene therapy materials. Nanomaterials for nucleic acid delivery offer an unprecedented opportunity to overcome these drawbacks; owing to their tunability with diverse physico-chemical properties, they can readily be functionalized with any type of biomolecules/moieties for selective targeting. Nucleic acid therapeutics such as antisense DNA, mRNA, small interfering RNA (siRNA) or microRNA (miRNA) have been widely explored to modulate DNA or RNA expression Strikingly. The CRISPR-Cas9 technology, one of the groundbreaking genome editing methods for addressing genetic disorders, has emerged as a powerful, precise, and efficient tool. However, its clinical translation remains hindered by challenges in delivery efficiency and targeting specificity. This review provides a comprehensive analysis of the structural features, advantages, and potential applications of various non-viral and stimuli responsive systems, examining recent progress to emphasize the potential to address these limitations and advance CRISPR-Cas9 therapeutics.We also summarize recent progress on stimuli-responsive nano formulations, a type of non-viral vector, to introduce precision and control in CRISPR-Cas9 delivery. The CRISPR/Cas9 gene-editing system has emerged as a revolutionary tool for accuracy genome modification, offering targeted disruption of antibiotic resistance genes, quorum sensing pathways, and biofilm-regulating factors. However, the clinical application of CRISPR-based antibacterials faces significant challenges, particularly in efficient delivery and stability within bacterial populations. Nanoparticles (NPs) present an innovative solution, serving as effective carriers for CRISPR/Cas9 components while exhibiting intrinsic antibacterial properties. Nanoparticles can enhance CRISPR delivery by improving cellular uptake, increasing target specificity, and ensuring controlled release within biofilm environments. Recent advances have demonstrated that liposomal CRISPR-Cas9 formulations can reduce Pseudomonas aeruginosa biofilm biomass by over 90% in vitro, while gold nano particle carriers enhance editing efficiency up to 3.5-fold compared to non-carrier systems.*

Keywords: CRISPR-Cas9; gene therapy; guide RNA, Cas9 enzyme, genome engineering, DNA repair, gene modification.