Lipid Nanocarriers as a Novel Platform for Precision Delivery of CRISPR-Based Gene Editing Systems and RNA Therapy in Glioblastoma

Elmira Aghaie[1], Nasrin Farahani[1*]
[1] Department of nanotechnology, Tehran medical sciences, Islamic Azad university
([*]corresponding author's E-mail: N.farahani@iautmu.ac.ir)

ABSTRACT

Glioblastoma (GBM) is one of the most aggressive and lethal brain tumors, characterized by high heterogeneity, rapid progression, and resistance to current therapeutic strategies. Standard treatments—including surgery, radiotherapy, and temozolomide chemotherapy—have limited efficacy, and median survival remains approximately 15 months. Among various molecular drivers of GBM, microRNA-10b (miR-10b) plays a central oncogenic role, being consistently upregulated in glioma cells while absent in normal brain tissue. Its inhibition demonstrates strong therapeutic potential. However, a major challenge is the efficient and safe delivery of gene-editing systems to intracranial tumors. Recent advancements in lipid nanoparticles (LNPs) have made them a promising platform for delivering mRNA and sgRNA for CRISPR-based therapies.

Keywords: Glioblastoma, Lipid Nanoparticles, Gene Editing, CRISPR-Cas9, microRNA-10b

Introduction Glioblastoma (GBM) is one of the most aggressive primary brain tumors, with a median patient survival of approximately 15 months despite maximal surgical resection, radiotherapy and temozolomide (TMZ) chemotherapy (1,2). GBM treatment is hindered by extensive heterogeneity and the persistence of therapy-resistant glioma stem cells (GSCs) (3). MicroRNA-10b (miR-10b) has emerged as a uniquely important therapeutic target, due to its consistent upregulation in malignant gliomas, absence in normal brain tissue, and essential for glioma growth and survival (4–12). Although miR-10b gene editing has shown therapeutic potential, safe and efficient in vivo delivery of CRISPR–Cas9 systems to intracranial tumors remains a major challenge. T**o overcome this challenge, researchers have developed lipid nanoparticles (LNPs) encapsulating Cas9 mRNA together with miR-10b–targeting sgRNAs, designated as miRTEN** (13-16).

Methods This review employed a structured literature analysis using recent peer-reviewed studies published in leading biomedical journals. Key databases including PubMed, Scopus, and Web of Science were systematically searched to identify advances in lipid nanoparticle design, CRISPR delivery strategies, and RNA-based therapeutics for glioblastoma.
Results Intracerebroventricular administration of miRTEN enabled broad and durable Cas9 mRNA expression and efficient miR-10b editing within both tumor cores and invasive

margins across multiple GBM models (5). miRTEN significantly reduced tumor growth, suppressed GSC proliferation, and increased tumor-cell death in a dose-dependent manner, with therapeutic effects correlating with the degree of miR-10b suppression (6). Combination therapy with TMZ further enhanced tumor inhibition, overcoming TMZ resistance and improving survival (17). In immunocompetent models, miRTEN activated robust antitumor immune responses, increased infiltration of cytotoxic $CD8^+$ T cells, and induced durable immune memory capable of rejecting rechallenged tumors (18,19). Safety evaluations confirmed that miRTEN selectively targets GBM cells while sparing normal brain tissue, with no evidence of neurotoxicity or impaired neuronal activity (9).

Conclusion As CRISPR-based therapeutics advance toward clinical application, **researchers** findings demonstrate that LNP-mediated delivery of Cas9 mRNA and sgRNAs enables safe and effective miR-10b gene editing in vivo. miRTEN shows strong therapeutic benefit as both monotherapy and in combination with standard-of-care treatment, offering a promising platform for advancing gene-editing and RNA-based therapies for GBM and other high-grade gliomas.

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