Engineering Multifunctional Lipid Nanocomplexes for Precision Glioblastoma Therapy: A Paradigm Shift in Treatment Strategies

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Malignant gliomas present a formidable challenge in the realm of medical treatment due to a multitude of constraining factors. The presence of the blood-brain barrier, the resistance encountered when delivering therapeutic agents specifically to tumor cells, and the resulting bleak prognosis all contribute to the complex task of managing this condition. To address these issues and capitalize on cellular targeting for enhanced precision and efficacy, nano-based therapeutic compounds have emerged as a promising approach. In this investigation, we have developed a novel strategy involving dual drug-loaded, multi-targeting liposomes to achieve effective and targeted delivery within an intracerebral glioma model. These multifunctional liposomes have been meticulously designed to encompass a standard anticancer drug, Temozolomide, in combination with a chemosensitizer O6-Benzylguanine. Additionally, the liposomes are armed with transferrin as a ligand, allowing them to bypass the formidable blood-brain barrier, and an anti-integrin antibody for precise targeting of U-87 MG Luc+ glioma tumor cells. Our engineered nano-liposomes have demonstrated excellent drug entrapment efficiency, with a particle size of 187±10 nm. These liposomes have undergone *in vitro* and *in vivo* testing to assess the pharmacokinetics of the nanocomposite in comparison to the pure drug combination. Notably, the functionalized liposomes exhibited remarkable cellular uptake, a phenomenon that further amplified the induction of glioma cell apoptosis. Furthermore, our pharmacokinetic analysis unveiled the efficient intracerebral uptake of the nanocomposite, which is accompanied by a controlled drug release over a span of 48 hours following intravenous administration. This is in stark contrast to the rapid clearance of pure Temozolomide from the brain within a mere 4 hours. These results signify a potential breakthrough, offering newfound hope for effective glioma treatment strategies.

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