**Endogenic Transferrin-Targeted Cell Membrane-Coated Biomimetic Lipo-complexes for Efficient Targeting and Enhanced Antitumor Efficacy in Orthotopic Glioblastoma**

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**Background and aims.** Due to the invasive growth of glioblastomas (GBM) and their resistance to conventional chemotherapy, the efficacy of GBM treatment remains limited. Biomimetic BBB-penetrating hybrid nanovehicles, engineered through homologous cell membrane fusion between cancer cells and protein corona (PC)-mediated liposomes coated with cancer cell membranes, have been explored for brain-targeted drug delivery.

**Methods.** T10 peptide-modified cell membrane-coated liposomes were used to construct an in situ transferrin (Tf) PC-mediated lipo-complex carrying a respiratory depressant agent (metformin, MET) and a photosensitizer (Chlorin, Ce6), creating a transferrin- and cancer cell-targeting delivery system (MET/Ce6@Lipo@CM@T10)..

**Results.** MET/Ce6@Lipo@CM@T10 possesses a spherical core–shell structure with uniform distribution while maintaining low systemic toxicity. Upon irradiation, MET/Ce6@Lipo@CM@T10 effectively inhibited cell proliferation and induced apoptosis via photodynamic therapy (PDT). Simultaneously, the loaded MET alleviated intracellular hypoxia caused by PDT, thereby enhancing anti-tumor efficacy. The establishment of an in vitro BBB model and 3D tumor spheroid experiments confirmed that MET/Ce6@Lipo@CM@T10 effectively crossed BBB and deeply accumulated within tumor tissues.



**Figure 1.** Schematic illustration of design and preparation of the MET/Ce6@Lipo@CM@T10 and enhanced photodynamic therapy of glioblastoma under dual-targeting by transferrin corona and cell membrane..

**Conclusion/Discussion.** *In vivo* animal experiments, MET/Ce6@Lipo@CM@T10 significantly inhibited tumor growth, promoted tumor necrosis and apoptosis, and demonstrated systemic safety. MET/Ce6@Lipo@CM@T10 demonstrated enhanced PDT effects on GBM, and will provide new insights and methods for GBM treatment.

**References:**

(1) Zhonggao Gao\*, et al, Acta Pharmaceutica Sinica B, 2025, in press.