

Anti-CD133 Ab/angiopep-2-conjugated immunoliposomes for targeting glioblastoma stem cells

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Glioblastoma (GBM) cancer stem cells (CSCs) are considered to associating with glioblastoma cancer initiation, drug (or radio) resistance and malignancy. GBM CSCs, which are identified as subpopulation of CD133⁺/ALDH1⁺, are known to show resistance to the most of chemotherapy and radiation therapy [1]. Angiopep-2 (An2) is targeted ligand to Low density lipoprotein receptor-related protein 1 (LRP1) in blood-brain barrier (BBB) [2] and anti-CD133-monoclonal antibody is targeted GBM CSCs surface [3]. We developed dual targeted immunoliposomes encapsulating with temozolomide as target specific drug delivery system for GBM CSCs therapy.

Liposomes were prepared with phospholipids by freeze-thawing method. Formulation of liposomes (LP) was composed of L- α -phosphatidylcholine from egg (EPC), 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[maleimide (polyethylene glycol)-2000] (ammonium salt) and cholesterol followed by anti-CD133 mAb and angiopep-2 conjugation to liposomes. The liposomes were characterized by measuring the size distribution and zeta potential. The encapsulation efficiencies of temozolomide determined by Bligh and Dyer extraction method. In vitro anticancer activity of anti-CD133-mAb/An2-conjugated immunoliposomes (ILP) encapsulating temozolomide in U87MG glioblastoma and their CSCs was determined by MTT assay, apoptosis assay, clonogenic assay and migration assay. The mean diameters of liposomes were 195.4 nm and 203.4 nm for the LP and the ILP, respectively. Zeta potentials were -5.30 mV and -1.61 mV for the LP and the anti-CD133-mAb/An2-ILP, respectively. The encapsulation efficiencies of gemcitabine were 94.3% and 99.2% for the LP and the anti-CD133-mAb/An2-ILP, respectively. Anti-CD133-mAb/An2-ILP encapsulating temozolomide increased cytotoxicity and

apoptosis to GBM CSCs and decreased colony formation and migration rate of GBM CSCs. The anti-CD133-mAb/An2-ILP encapsulating temozolomide is expected to be a potential agent to effectively eradicate the GBM CSCs properties *in vitro* and *in vivo*.

Keywords: Glioblastoma stem cells; Targeting; Liposomes; Temozolomide

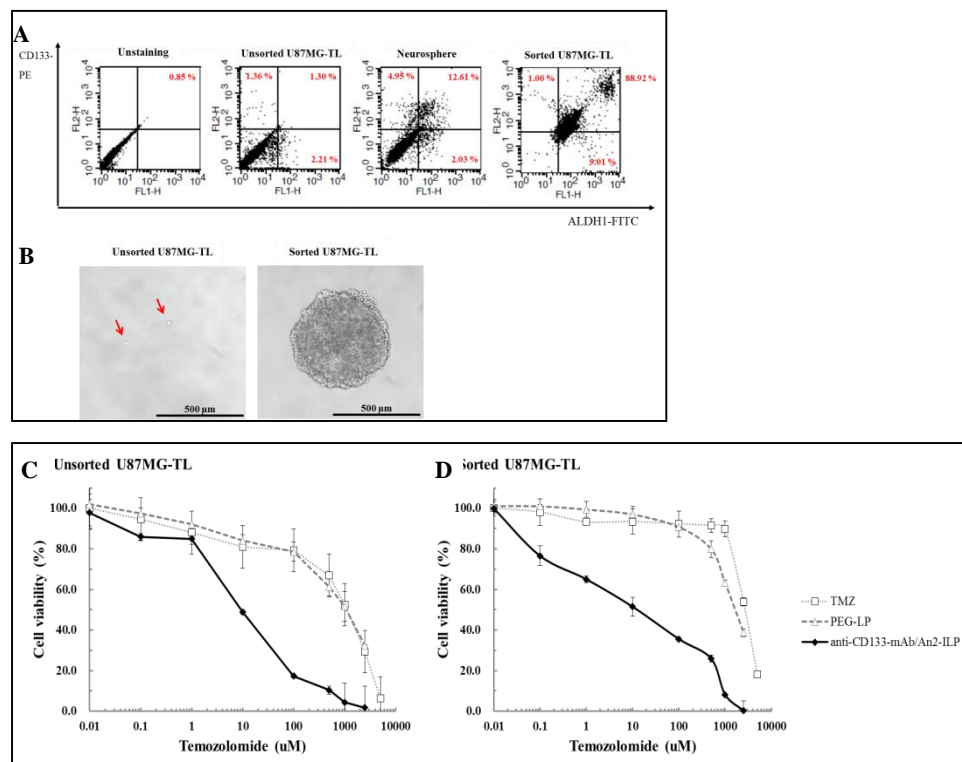


Fig. 1. Characterization of U87MG-TL glioblastoma and their CSCs. Flow cytometry analysis (A) and representative photographs of secondary spheres image (B) and Growth-inhibitory effects of U87MG-TL glioblastoma (C) and their CSCs (D).

References

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