

Anti-Tumor Activity of mApoE-Functionalized Drug-Loaded Liposomes through Glioblastoma Stem Cells Targeting

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Glioblastoma (GBM) is among the deadliest of all human cancers. Even in case of a promising response to initial treatments, recurrence is unavoidable and fatal, with less than 5% of the patients surviving beyond 5 years. To control tumor growth, and ultimately cure patients, it is essential to develop novel treatments to selectively kill therapy-resistant cells. The radio- and chemo- resistance of GBM Stem-like Cells (GSCs) together with their innate tumor-initiating aptitude, make this cell population a crucial target for effective therapies. However targeting GSCs is hardly difficult and complex, due the presence of the Blood Brain Barrier (BBB) and to their infiltrative nature arousing their dispersion within the brain parenchyma. Using liposomes as carriers for doxorubicin (DOXO-LIPs) and specifically surface-functionalized with the mApoE peptide that allows Low-Density Lipoprotein Receptor (LDLR) engagement, we provide in a orthotopic patient-derived xenograft (PDX) preclinical model the proof of concept for a multi-task strategy able to facilitate drug crossing through BBB and to ensure GSCs targeting. Our results indicates that the encapsulation into liposomes prevents DOXO toxicity on BBB cells. When administered to PDXs mApoE-DOXO-LIPs trigger GSC apoptosis resulting in a remarkable reduction of tumor growth and invasiveness. Finally, the concomitant administration of a single dose radiation (2Gy) enhanced mApoE-DOXO-LIP anti-tumor effects by altering BBB permeability and enhancing the expression of LDL-R on both BBB and GSCs. Therefore, mApoE-DOXO-LIPs, in synergy with radiations, can be proposed as promising nanotherapeutic strategy against GBM.