Documents

Bozzato, E.[a] , Tsakiris, N.[a] , Paquot, A.[b] , Muccioli, G.G.[b] , Bastiancich, C.[a c d] , Préat, V.[a]

Dual-drug loaded nanomedicine hydrogel as a therapeutic platform to target both residual glioblastoma and glioma stem cells

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[a] Université Catholique de Louvain, Louvain Drug Research Institute, Advanced Drug Delivery and Biomaterials, Brussels, Belgium

[b] Université Catholique de Louvain, Louvain Drug Research Institute, Bioanalysis and Pharmacology of Bioactive Lipids Research Group, Brussels, Belgium

[c] Aix-Marseille Univ, CNRS, INP, Institut Neurophysiopathol, Marseille, France

[d] Department of Drug Science and Technology, University of Turin, Turin, Italy

Abstract

Glioblastoma (GBM) recurrences are inevitable, and mainly originate from residual tumor cells and the presence of glioma stem cells (GSC) around the resection cavity borders. We previously showed that the local treatment of GBM with nanomedicine-based Lauroyl-gemcitabine lipid nanocapsules (GemC12-LNC) hydrogel delayed tumor onset in various preclinical models and can be used as a scaffold to deliver multiple drugs. However, it does not inhibit tumor relapse in the long-term. In this work, we aim at encapsulating an anti-GSC molecule in the GemC12-LNC hydrogel to eliminate both GBM cells and GSC. We performed a screening on GBM cell lines (GL261 and U-87 MG) and patient-derived GSC (GBM9) to select the anti-GSC molecule that could act synergically with GemC12. Based on our results, salinomycin (Sal) and curcumin (Cur) were selected for further development. Both GemC12-Sal-LNC and GemC12-Cur LNC showed similar size (55 nm), zeta potential (- 2 mV) and viscoelastic properties compared to the GemC12-LNC hydrogel. Encapsulation efficiency was above 95 %. Moreover, the GemC12-Sal-LNC hydrogel was stable for at least 6 months and released both drugs over 30 days in vitro. Both hydrogels inhibited the growth of GL261 and U-87 MG spheroids. Flow cytometry analysis showed that Sal reduced the GSC population in GL261 and U-87 MG cells. Our results show that the co-encapsulation of Sal in the GemC12-LNC hydrogel can reduce both GBM cells and GSC, and therefore might be promising to avoid the onset of GBM recurrences. © 2022 Elsevier B.V.

Author Keywords

Gemcitabine; Glioblastoma; Glioma stem cells; Hydrogel; Local delivery; Salinomycin

Index Keywords

curcumin, hydrogel, salinomycin, curcumin, lipid; animal cell, antineoplastic activity, Article, cancer inhibition, controlled study, flow cytometry, GL261 cell line, glioblastoma, glioma stem cell, growth inhibition, human, human cell, in vitro study, mouse, nanoencapsulation, nanomedicine, nonhuman, particle size, viscoelasticity, zeta potential, brain tumor, cancer stem cell, glioma, hydrogel, metabolism, nanomedicine, pathology, procedures, tumor cell line; Brain Neoplasms, Cell Line, Tumor, Curcumin, Glioblastoma, Glioma, Humans, Hydrogels, Lipids, Nanomedicine, Neoplastic Stem Cells

Correspondence Address

Bastiancich C.; Université catholique de Louvain, Avenue Mounier, 73, Belgium; email: chiara.bastiancich@univ-amu.fr

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