1. Record Nr. TD17002309

Autore	M. Tamborini
Titolo	A NANOTECHNOLOGY APPROACH FOR GLIOBLASTOMA TARGETED THERAPY [Tesi di dottorato]
Editore	Università degli Studi di Milano, 2016-01-11
Lingua di pubblicazione	Inglese
Formato	Tesi di dottorato
Livello bibliografico	Monografia
Note	diritti: info:eu-repo/semantics/openAccess In relazione con info:eu-repo/semantics/altIdentifier/hdl/2434/351946
Sommario	Glioblastoma multiforme (GBM) is an extremely aggressive type of glioma. Life expectancy is around two years after diagnosis, due to recidivism and to the presence of the blood brain barrier (BBB) restricting the amount of drugs which arrive at the residual cancer cells, thus contributing to chemotherapies failure. To overcome the impediment imposed by the BBB, we have investigated the use of nanotechnologies in synergy with radiotherapy as a prospective strategy for GBM treatment. We have used poly(lactic-co-glycolic acid) (PLGA) nanoparticles (PNP) conjugated to the peptide chlorotoxin (CTX), which has been shown to recognize and selectively bind to glioma cells. Silver nanoparticles have been encapsulated inside the functionalized nanoparticles (Ag-PNP-CTX), to allow detection of cellular uptake and quantification by means of confocal microscopy, both in vitro and in vivo. In vitro experiments, involving 3 different human glioblastoma cell lines, have shown that the cytoplasmic uptake of Ag-PNP-CTX is higher than that of non-functionalized nanoparticles. Experiments performed in vivo have shown high efficiency of Ag-NP-CTX particles in targeting tumor cells; however, they have been shown to be scarcely able to cross the blood brain barrier at the healthy brain level, where scattered metastatic cells are present too. A single x-rays administration on

	the whole brain, carried out twenty hours before the injection of the nanoparticles, has been shown to increase the levels of expression of the CTX targets MMP-2 e ClC-3. Moreover, through an alteration of BBB permeability, it has been shown to potentially increase the quantity of internalized Ag-PNP-CTX also in dispersed cells, and to lead to significant results in inhibiting tumor growth in vivo. Notably, the administration of Ag-PNP-CTX to irradiated tumor cells decreases the MMP-2 extracellular activity. By targeting scattered GBM cells and limiting MMP-2 activity, the synergic use of nanovectors conjugated with CTX and radiotherapy may represent an efficient therapeutic approach to GBM treatment.
Localizzazioni e accesso	http://memoria.depositolegale.it/*/http://hdl.handle.net/2434/351946