Development of multifunctional lipid nanocapsules for the co-delivery of paclitaxel and CpG-ODN in the treatment of glioblastoma

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Résumé en anglais	In this work, multifunctional lipid nanocapsules (M-LNC) were designed to combine the activity of the cytotoxic drug paclitaxel (PTX) with the immunostimulant CpG. This nanosystem, consisting of modified lipid nanocapsules coated with a cationic polymeric shell composed of chitosan (CS), was able to allocate the hydrophobic drug PTX in the inner oily core, and to associate onto the surface the genetic material CpG. The CS-coated LNC (CS-LNC), showed a narrow size distribution with an average size of 70nm and a positive zeta potential (+25mV). They encapsulated PTX in a high amount (98%), and, due to the cationic surface charge, were able to adsorb CpG without losing stability. As a preliminary in vitro study, the apoptotic effect on GL261 glioma cells was investigated. The drug-loaded CS-LNC exhibited the ability to interact with glioma cells and induce an important apoptotic effect in comparison with blank systems. Finally, the M-LNC made of CS-LNC loaded with both CpG and PTX were tested in vivo, injected via convention enhanced delivery (CED) in GL261-glioma-bearing mice. The results showed that the overall survival of mice treated with the M-LNC was significantly increased in comparison with the control, Taxol(®), or the separated injection of PTX-loaded LNC and CpG. This effect was also confirmed by magnetic resonance imaging (MRI) which revealed the reduction of tumor growth in the animals treated with CpG and PTX-loaded M-LNC. All these findings suggested that the developed M-LNC could potentiate both CpG immunopotency and PTX antitumor activity by enhancing its delivery into the tumor microenvironment.
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