NIR LASER-RESPONSIVE FOLATE-TARGETED GOLD NANORODS AS EFFICIENT THERANOSTIC TOOL FOR OSTEOSARCOMA TREATMENT

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Folate-targeted gold nanorods (GNRs) are here proposed as selective theranostic agents for osteosarcoma treatment. Taking advantage of the attractive physiochemical and optical properties of GNRs they can be proposed as effective and selective platform to obtain a targeted intracellular drug release, photothermal therapy and cancer imaging, which may improve therapeutic outcomes of osteosarcoma. An amphiphilic polysaccharide based graft-copolymer, henceforth named INU-LA-PEG-FA, and an amino derivative of the α,β-poly(N-2-hydroxyethyl)-D,L-aspartamide functionalized with folic acid (PHEA-FA), have been synthesized to act as coating agents for GNRs. The obtained polymer-coated GNRs were characterized in terms of size, shape, zeta potential, chemical composition, aqueous stability. They protected the anticancer drug nutlin-3 in human plasma and were able to deliver it efficiently in different physiological media. The proposed systems selectively exert their toxic effect towards U2OS cancer cells expressing high levels of FRs compared with normal human bronchial epithelial cells (16HBE) and human dermal fibroblasts (HDFa). Moreover, we report the ability of the nanosystems of efficiently controlling drug release upon NIR laser irradiation and of acting as an excellent hyperthermia agent as well as Two Photon Luminescence imaging contrast agents. The proposed folate-targeted GNRs have also been tested in terms of chemoterapeutic and thermoablation efficacy on tridimensional (3-D) osteosarcoma models which better mimic cancer microenvironments and therefore offer the promise of improving clinical efficacy. Overall, the proposed folate targeted GNRs displayed outstanding anticancer activity on bidimensional and on 3-D tumor models, making them appealing multimodal agents for image-guided therapies based on localized hyperthermia and chemoterapy of solid tumors.

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