

MULTIFUNCTIONAL CONTRAST AGENTS FOR MOLECULAR IMAGING OF PROSTATE CANCER

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Development of efficacious receptor-targeting contrast agents is particularly important for early detection of prostate cancers. When using non-invasive magnetic resonance imaging (MRI) for molecular imaging, sensitivity and specificity are critical issues. A multimodal approach such as MRI/optical and MRI/positron emission tomography can solve the problems associated with individual imaging modality. In our previous study, a near-infrared fluorescent bombesin (BBN) conjugate, AlexaFluro680-BBN[7-14], has shown high efficacy for gastrin releasing peptide receptor (GRPR) targeted imaging in human cancer mouse models. In this work, we report results on the synthesis and characterization of hybrid nanoparticle contrast agents AlexaFluro750-BBN[7-14]-SPIO and Gd-DOTA-BBN[7-14]-SPIO for dual-modality molecular imaging of prostate cancers. The nanoparticles consist of a biocompatible super-paramagnetic iron oxide (SPIO) core and AlexaFluro750-BBN or Gd-DOTA-BBN conjugates on the surface of SPIO. The characterizations were performed by IC₅₀ (the half maximal inhibitory concentration), Prussian-blue staining reaction, atomic force microscope (AFM) imaging and fluorescence microscopic imaging in PC-3 prostate cancer cells. MRI relaxivity enhancements were determined using spin-echo sequences on 7T MRI. In vitro and in vivo imaging efficacy was evaluated and compared to non-targeted contrast agents, i.e. Gd-DTPA and SPIO, using MRI/optical imaging in PC-3 cells and SCID tumor xenografts. Our results show that the BBN-based multifunctional SPIO nanoparticles demonstrated high binding affinity and specificity and subsequent retention of the ligands in GRPR over-expressing prostate cancer cells via agonist initiated receptor-mediated endocytosis. This agonist initiated receptor-mediated endocytosis approach may offer a dynamic mechanism on nanoparticle accumulation and signal amplifications in cancer cells.