Biomaterials 33 (2012) 9232–9238

Contents lists available at SciVerse ScienceDirect

Biomaterials

journal homepage: www.elsevier.com/locate/biomaterials

PEG modified $BaGdF_5$:Yb/Er nanoprobes for multi-modal upconversion fluorescent, *in vivo* X-ray computed tomography and biomagnetic imaging

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ARTICLE INFO

Article history:
Received 26 August 2012
Accepted 11 September 2012
Available online 1 October 2012

Keywords:
Upconversion
Nanoparticle
Fluorecent bio-imaging
X-ray computed tomography
Magnetic property

ABSTRACT

Herein, a multi-functional nanoprobe of polyethylene glycol (PEG) modified $BaGdF_5$:Yb/Er upconversion nanoparticles (UCNPs) for tri-modal bioimaging of fluorescence, computed X-ray tomography (CT), and magnetic application is demonstrated for the first time. The PEG-modified $BaGdF_5$:Yb/Er UCNPs with optimal small size were synthesized by a facile one-pot hydrothermal method. The as-designed single-phase nanoprobe presents near-infrared to visible upconversion emissions in UC fluorescent bioimaging of HeLa cell. Importantly, we have demonstrated *in vivo* CT images with enhanced signals of spleen of a mouse for 2 h, indicating the UCNPs can be successfully used as CT contrast agent for improving the detection of splenic diseases. In addition, these UCNPs also exhibit excellent intrinsic paramagnetic property which can be also for magnetic imaging. Therefore, our results indicate that a tri-modal nanoprobe served as fluorescent/CT/magnetic bioimaging can be realized using the PEG-modified $BaGdF_5$:Yb/Er UCNPs with very low cytotoxicity and long circulation time, which would be very useful in a variety of biomedical application fields.

1. Introduction

In recent years, bioimaging study has attracted much attention due to its ability to visualize and understand many functions in various biosystems ranging from specific molecules to tissues. Bioimaging techniques such as fluorescent imaging [1–5], computed X-ray tomography (CT) [6–9], and magnetic resonance imaging (MRI) [10–13] have played important roles in the area of bioimaging. Among them, CT is a well-established clinical diagnosis technique that is capable of providing high-resolution 3D information of the anatomic structure of tissues based on the differential X-ray absorption ability of the tissues [7]. However, owing to the low sensitivity to soft tissues, its applications in disease detection have been greatly limited. In contrast to CT, magnetic resonance imaging (MRI) can provide unsurpassed 3D soft tissue details and functional information due to the non-ionizing radiation. Although CT and MRI techniques possess many advantages, both of them suffer from limited planar resolution and are not suitable for cellular level imaging, which can be solved by fluorescent imaging [14,15]. Therefore, a synergistic combination of fluorescence, CT and MRI contrast agents in single system, which can help combine the advantages of each, while avoiding the disadvantages of the other, faces a great challenge.

So far, there are only a few results on the trimodal nanoprobe for bioimaging. For instance, a fluorescence/CT/MRI trimodal system based on paramagnetic CdS:Mn/ZnS quantum dots (QDs) was reported [16]. However, these QDs suffer from some inherent problems including the high toxicity and low tissue penetration owing to the excitation of ultraviolet (UV) light, which limited their application as imaging probes. Compared with the conventional fluorescence probes, such as organic dyes and QDs, near-infrared (NIR)-excited upconversion nanoparticles (UCNPs) possess many advantages, including low-autofluorescence, deep tissue penetration, large anti-Stokes shifts, high photostability, and low toxicity [17–23]. Among all of the developed UC hosts, fluorides are considered as the most efficient host lattice for UC luminescence owing to their low phonon energy [24]. Most reports have been focused on the development of lanthanide doped $NaYF_4$ UCNPs for fluorescent bioimaging of cells and tissues *in vitro* and *in vivo* [25–29]. Very recently, a PEGylated NaY/GdF_4:Yb, Er, Tm@SiO_2-Au@PEG_{5000} system for trimodal bioimaging was designed by using co-thermolysis method in non-hydrolytic solvents and multi-step

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http://dx.doi.org/10.1016/j.biomaterials.2012.09.019