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Gd^{3+} complex-modified $NaLuF_4$-based upconversion nanophosphors for trimodality imaging of NIR-to-NIR upconversion luminescence, X-Ray computed tomography and magnetic resonance

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ABSTRACT

Multimodality molecular imaging has recently attracted much attention, because it can take advantage of individual imaging modalities by fusing together information from several molecular imaging techniques. Herein, we report a multifunctional lanthanide-based nanoparticle for near-infrared to near-infrared (NIR-to-NIR) upconversion luminescence (UCL), X-ray computed tomography (CT) and T_1-enhanced magnetic resonance (MR) trimodality *in-vivo* imaging. By careful selection of the lanthanide elements, core–shell structured lanthanide-based nanoparticles, $NaLuF_4$:Yb^{3+},Tm^{3+}@SiO_2-GdDTPA nanoparticles (UCNP@SiO_2-GdDTPA) have been designed and synthesized. We also prove that the application of UCNP@SiO_2-GdDTPA for NIR-to-NIR UCL, CT and MRI multi-modality *in-vivo* imaging can be established successfully. In addition, the biological toxicity of UCNP@SiO_2-GdDTPA is evaluated by the methyl thiazolyl tetrazolium (MTT) assay and histological analysis of viscera sections.

1. Introduction

Molecular imaging techniques, such as magnetic resonance imaging (MRI), X-ray computed tomography (CT), fluorescence microscopy, and positron emission tomography (PET) play an important role in medicine and biomedical research [1–4]. But information obtained from single modal molecular imaging cannot satisfy the higher requirements on the efficiency and accuracy for clinical diagnosis and medical research, due to its limitation and default rooted in single molecular imaging technique itself [5]. For example, fluorescence microscopy with high sensitivity is often restricted because of its relatively poor resolution, whereas CT and MR imaging with a high spatial resolution are of insufficient sensitivity. The information gathered from fluorescence microscopy, CT and MR imaging techniques together could solve the problems of sensitivity and resolution that arise from the selection of a particular imaging modality [6–9]. Thus, multimodality imaging will provide more complementary, effective and accurate information about the physical, anatomical structure and the physiological function for diagnosis and research.

Nanotechnology has greatly promoted the development of the multimodal contrast agent for CT/MRI, PET/optical and optical/MRI molecular imaging, because of its ability to integrate multiple functions to a single particle, with subtle structures and molecular composition on the nanoscale [10–15]. Resulting from their special 4f electron structure and rich optical-magnetic properties [16–18], lanthanide-based nanoprobes have attracted increasing attention in multimodal molecular imaging. In particular, lanthanide-based nanoparticles co-doped with Yb^{3+} and Er^{3+}/Tm^{3+} show unique upconversion luminescence (UCL), which promises a high signal-to-noise ratio (SNR) and deep light penetration for small animal imaging [19–23]. Therefore, his kind of upconversion materials are regarded as a new generation of luminescent labels for bio-applications [24,25]. Moreover, some lanthanide ions with unpaired f electrons are paramagnetic and have been used as contrast agents for MR imaging [26–30]. To date, lanthanide-doped nanoparticles have been applied successfully as probes for dual-modality or trimodality imaging, combining PET, MRI and UCL imaging [31–33]. Recently, several cases of multimodal imaging involving CT imaging have been reported using lanthanide-doped nanoparticles as probes [34]. Compared to the iodinated derivatives, lanthanide ions have a higher atomic number and strong X-ray attenuation, and they are better suited for CT imaging. Introducing CT to the UCL/MR imaging, it will offer more information on the spatial resolution, especially to position of soft tissues [35].

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