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FULL PAPER

Highly Emissive Nd^{3+}-Sensitized Multilayered Upconversion Nanoparticles for Efficient 795 nm Operated Photodynamic Therapy

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Photodynamic therapy (PDT) is a noninvasive and site-specific therapeutic technique for the clinical treatment of various of superficial diseases. In order to tuning the operation wavelength and improve the tissue penetration of PDT, rare-earth doped upconversion nanoparticles (UCNPs) with strong anti-stokes emission are introduced in PDT recently. However, the conventional Yb^{3+}-sensitized UCNPs are excited at 980 nm which is overlapped with the absorption of water, thus resulting in strong overheating effect. Herein, a convenient but effective design to obtain highly emissive 795 nm excited Nd^{3+}-sensitized UCNPs ($NaYF_4$:Yb,Er@$NaYF_4$:$Yb_{0.1}Nd_{0.4}$@$NaYF_4$) is reported, which provides about six times enhanced upconversion luminescence, comparing with traditional UCNPs ($NaYF_4$:Yb,Er@$NaYF_4$). A colloidal stable and non-leaking PDT nanoplatform is fabricated later through a highly PEGylated mesoporous silica layer with covalently linked photosensitizer (Rose Bengal derivative). With as-prepared Nd^{3+}-sensitized UCNPs, the nanoplatform can produce singlet oxygen more effective than traditional UCNPs. Significant higher penetration depth and lower overheating are demonstrated as well. All these features make as-prepared nanocomposites excellent platform for PDT treatment. In addition, the nanoplatform with uniform size, high surface area, and excellent colloidal stability can be extended for other biomedical applications, such as imaging probes, biosensors, and drug delivery vehicles.

1. Introduction

Light/laser with high spatial resolution and strong operability has long been adopted for healthcare purpose and the treatment of various superficial diseases.[1] In particular, light can activate a class of chemicals named photosensitizer to generate cytotoxic reactive oxygen species, typically singlet oxygen ($^1O_2$) to damage cells and tissues.[2] This noninvasive and site-specific therapeutic technique known as photodynamic therapy (PDT) can provide high therapeutic efficacy and less side effects compared with radiotherapy and chemotherapy, and has been widely explored for cancer therapy over the past three decades.[3] However, the further development of PDT was largely limited by the potency of the photosensitizer. The excitation wavelength of the clinically used photosensitizers is around 630–690 nm at present,[1a] which is not in the near-infrared (NIR) window (750–900 nm), thus leads to a limited penetration depth of human tissue.[4] The difficulty for improvement lies in the fact that photosensitizers with NIR absorption cannot produce $^1O_2$ efficiently, while the others with high $^1O_2$ quantum yield need to be excited at visible light.[5]

Fortunately, the great improvement of upconversion nanoparticles (UCNPs) provides an alternative way to overcome this problem.[6] UCNPs can convert low energy NIR light to high energy visible light by multiple photon absorption or energy transfer,[7] thus can excite the photosensitizers indirectly with NIR light, which allows improved tissue penetration depth of PDT treatment.[8] However, traditional UCNPs sensitized with Yb^{3+} need to be excited at the wavelength of 980 nm, which is overlapped with the absorption of water therefore result in strong overheating effect and low tissue penetration.[9] Several efforts have been made in tuning the excitation wavelength of UCNPs into the biological NIR window,[10] and the doping of Nd^{3+} was found to be the most promising one. First, Nd^{3+} doping enables the UCNPs to be sensitized at around 800 nm where the heating effect is minimized and the tissue transparency is maximal. Second, the absorption cross section of Nd^{3+} is one order of magnitude higher than that of Yb^{3+}, which

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