Mesoporous carbon@silicon-silica nanotheranostics for synchronous delivery of insoluble drugs and luminescence imaging

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A hierarchical theranostic nanostructure with carbon and Si nanocrystals respectively encapsulated in the mesopores and within the framework of mesoporous silica nanoparticles (CS-MSNs) was constructed by a bottom-up self-assembly strategy combining an in situ one-step carbonization/crystallization approach. CS-MSNs exhibited narrow size distribution, high payload of insoluble drugs and unique NIR-to-Vis luminescence imaging feature. The bio-conjugated CS-MSNs with a PEGylated phospholipid compound and hyaluronic acid showed excellent dispersivity and could specifically target cancer cells overexpressing CD44, deliver insoluble drugs into these cells and consequently kill them effectively, and also fluorescently image them simultaneously in a unique and attractive NIR-to-Vis luminescence imaging fashion, providing a promising opportunity for cancer theranostics.

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1. Introduction

According to the specific needs for the treatment of major diseases (typically cancers and cardiovascular diseases), such as i) the early detection and diagnosis, ii) the targeted delivery of therapeutic agents, and iii) the synchronous monitoring of therapeutic responses, the “theranostic” concept has been introduced in clinics to combine diagnostic and therapeutic capabilities into a single agent. The occurrence of nanotechnology has offered a number of advanced nano-platforms with combined imaging and therapeutic functions. Subsequently, “theranostic nanomedicine”, integrating the virtues of advanced imaging and therapeutic nano-platforms, is rapidly growing into a promising medical methodology, and has drawn much attention in the past few years [1–3]. Great efforts have been devoted toward theranostic nanomedicine, however there are still challenges in increasing the payload of specific therapeutic agents, typically water-insoluble drugs, improving the imaging quality, enhancing the targetability, etc.

Mesoporous silica nanoparticles (MSNs) have been qualified as a new type of excellent theranostic nano-platform, thanks to their unique features, such as tunable porosity, high surface area, large pore volume, facile functionalization, good biocompatibility, high physicochemical and biochemical stability, etc [4–6]. A broad range of imaging and therapeutic agents, such as superparamagnetic iron oxide nanoparticles, quantum dots, upconversion nanoparticles, Gd complexes, fluorescein molecules, genes, chemotherapeutic drugs, and so on, have been loaded/grafted/encapsulated into MSNs to achieve theranostic purposes [7–13]. However, as far as drug loading is concerned, the loading capacity of MSNs for water-insoluble anti-cancer drugs, which can be hardly loaded into hydrophilic pore network of MSNs, should be greatly enhanced for the effective drug delivery, because about 40% of anti-cancer drugs are hydrophobic but frequently more effective than the others.

Biological optical imaging is one of the most common imaging modalities for disease diagnosis. The present organic fluorescent dyes or most of luminescent quantum dots containing heavy metal ion(s) as bio-imaging agents have poor biochemical stability or potential toxicity, respectively. Upconversion nanoparticles (UCNPs) usually containing rare-earth heavy elements and exhibiting outstanding upconversion luminescence have been developed for applications in biological imaging and drug delivery [14–18]. However comparatively, Si nanocrystals are more biodegradable and non-cytotoxic because of absence of heavy elements and non-toxicity of degradation products [19], and also have been recently discovered capable of luminescence in the visible region through the multi-photon excitation of near infrared (NIR) light, which is highly desired in medical imaging to avoid the photo-damage and the disturbance by tissue auto-luminescence [20,21]. Therefore, the combination of MSNs with Si nanocrystals would be a highly promising theranostic platform, which, however, has never been