**Multifunctional nanocomposites with sequential tumor acidity responsiveness for cancer photodynamic therapy and imaging**

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Introduction.

During the last decades, multifunctional polymeric nanoparticles with core/shell structures have been widely studied as drug and/or imaging agent carriers for tumor therapy and diagnostics (theranostics).1 However, it is a big challenge for these nanoparticles to target the tumor site and release their payloads after reaching tumor sites. To solve this problem, much work has been done to endow these nanoparticles responsiveness to tumor environments (so called smart drug delivery carriers). pH is a frequently used stimulus to trigger the release of therapeutic and/or imaging agents from nanoparticles, because tumor extracellular pH (ranging from 6.5-7.0) and intracellular pH (ranging from 5.0-6.5) are generally lower than physiological pH (pH 7.4).2,3

Methods.

The core/shell-structured nanoplatform was constructed via self-assembly of a Ce6-conjugated polypeptide ligand and superparamagnetic iron oxide nanoparticles.

Results and discussion.

Sequential tumor acidity-responsive nanoplatform has been successfully developed for pH-activated bimodal imaging and PDT. During blood circulation, this nanoplatform can effectively suppress phototoxicity, prolong circulation time, and target the tumor site. Once the nanoplatform reaches the tumor location (pH < 6.8), this nanoplatform improves tumor accumulation and cellular internalization via pH-induced surface charge switching and then is further disassembled in more acidic intracellular compartments, which facilitates fluorescence and singlet oxygen generation of the photosensitizer (Ce6). This nanoplatform can be utilized to visualize human hepatoblastoma xenograft tumors implanted in mice through pH-recognizing T2-weighted MR/NIRF imaging without the use of targeting ligands, which also reveals significantly enhanced tumor retention in comparison to pH-insensitive nanoparticles. Moreover, this nanoplatform exhibits excellent in vivo antitumor efficiency, which makes it a powful tool for tumor theranostics.

Conclusion.

A multifunctional nanoplatform was developed for tumor acidity-activated PDT and cancer diagnosis. This nanoplatform has excellent stability in various physiological conditions and can promote cellular uptake, thus effectively killed cancer cells by pH-triggered charge-reversal in the acidic tumor microenvironment. In addition, this dual pH-responsive nanoplatform acts as a bimodal imaging nanoprobe for tumor imaging and enhanced tumor accumulation. Moreover, this nanoplatform exhibits excellent tumor inhibition ability in vivo.

**References**

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