NIR-Triggered Tumor-Selective Photodynamic Therapy Using Upconversion Nanoparticle Based Nanoassemblies

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Photodynamic therapy (PDT) has been widely applied to oncotherapy because of its minimally invasive nature and spatiotemporally controlled treatment capability. However, the limited tissue-penetration depth of visible light prevents the broad clinical application of PDT. Recently, lanthanide ion-doped upconversion nanoparticles (UCNPs), which absorb near-infrared (NIR) light and subsequently emit the high-energy visible light, have been utilized as nanotransducers for deep-tissue PDT in vivo.[2] However, such PDT agents still have side effects due to deficiencies in selective accumulation at tumor sites and unavoidable activation of photosensitizers under white-light exposure or by selfcatalyzed reactions. As a result, patients are required to avoid exposure to daylight, which increases the burden of patients undergoing the PDT treatment.[3] Herein, we developed tumor-pH-sensitive photodynamic nanoagents (PPNs) comprised of self-assembled photosensitizers grafted pH-responsive polymeric ligands and UCNPs. The PPNs are negatively charged without any discernible photoactivity at normal blood pH of $\approx$7.4, but can quickly switch their surface charge from negative to positive at an extracellular tumor pH of $\approx$6.5, and are further disassembled into individual UCNPs at intracellular tumor endo/lysosome pH ($\approx$5.5). This disassembly process promotes the dissociation of the aggregated photosensitizers (self-quenched state) into extended free molecules (de-quenched state), enabling significantly enhanced photoactivity of the photosensitizers. Upon NIR irradiation, upconverted emission light from the UCNPs can induce the photoactivity of the free photosensitizers in acidic tumor microenvironment. Moreover, the strong upconversion luminescence from the PPNs can be utilized for imaging-guided deep PDT. Both in vitro and in vivo results indicate that these PPNs can serve as a potentially new class of PDT agent for use in future cancer theranostics based on their ability to overcome limitations associated with conventional PSs, such as limited tissue-penetration depth, deficiencies in tumor-cell-targeting ability, and inevitable side effects observed in normal tissues.

References

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