A Multifunctional Theranostic Platform Based on Phthalocyanine-Loaded Dendrimer for Ovarian Cancer Treatment

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Purpose
To develop a theranostic nanomedicine platform that will enable maximal surgical resection through imaging of ovarian cancer tumor margins, and can also be employed intraoperatively to mediate photodynamic therapy (PDT), thereby eradicating occult microscopic tumors.

Methods
Owing to the outstanding near-infrared (NIR) optical properties, phthalocyanines (Pc) have promising potential as theranostic agents for fluorescence imaging and noninvasive treatment of deep cancer tumors by PDT. Nevertheless, clinical application of phthalocyanines is substantially limited by poor water solubility, aggregation and insufficient selectivity for cancer cells. The development of the theranostic platform was achieved by the initial encapsulation of monosubstituted phthalocyanine into PPI dendrimer followed by the modification of the dendrimer surface with polyethylene glycol and LHRH peptide to improve its biocompatibility and tumor cell selectivity. The developed platform was extensively characterized and tested both in vitro and in vivo.

Results
The developed nanocarriers have an average diameter of 62.3 nm and narrow size distribution. The drug encapsulation efficiency was 20% w/w, and the synthesized phthalocyanine derivative entrapped in the dendrimer-based nanocarrier exhibits a distinct NIR absorption (700 nm) and fluorescence emission (710 and 815 nm), required for an efficient PDT and fluorescence imaging. It was demonstrated that subcellular localization in vitro and organ distribution in vivo of the developed nanocarrier can be determined based on the intrinsic fluorescence properties of encapsulated phthalocyanine, validating its role as an imaging agent. The imaging experiments revealed that the LHRH targeted nanocarrier is capable of efficient internalization into cancer cells in vitro as well as in vivo tumor accumulation when intravenously administered into mice. Finally, the prepared formulation exhibited a low dark cytotoxicity while the light irradiated cancer cells transfected with the theranostic agent resulted in a significant decrease in cell viability (IC50 = 0.9 μg/mL) through excessive generation of toxic reactive oxygen species.

Conclusion
We developed a simple and effective approach for constructing a novel theranostic platform. Animal and in vitro studies revealed that the synthesized multifunctional nanocarrier is a good candidate, with excellent imaging and tumor-targeting abilities, for NIR fluorescence image-guided surgery and PDT treatment of ovarian cancer.