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• HIGHLIGHTS •

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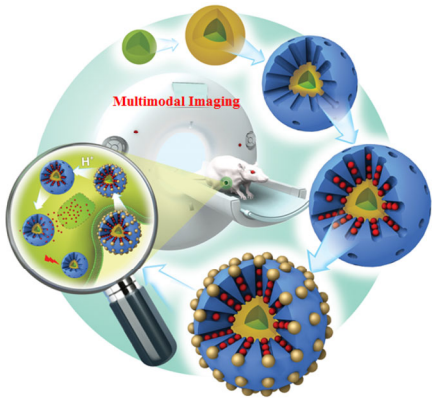
A novel upconversion nanotheranostic agent for multi-modality imaging-guided chemotherapy with on-demand drug release

Lanthanide-doped upconverting nanoparticles (UCNPs) are a unique type of phosphor, which could convert two or more low-energy near-infrared (NIR) photons into a high-energy photon. This unique feature endows UCNPs with great potentials in a variety of applications, including solid-state lasers, three-dimensional flat panel displays, and especially bio-imaging. Most importantly, with proper surface modification and functionalization, UCNPs have been employed as anticancer drug nanocarriers in malignant tumor treatment. However, anticancer drugs usually release before they reach the target cancer cells, resulting in significant side effects and limited treatment efficiency. To tackle this issue, it is highly desirable to develop stimuli-responsive drug-delivery system based on UCNPs which could serve as contract agents for bio-imaging and on-demand drug release, but it remains a great challenge.

Recently, Hongjie Zhang's group at Changchun Institute of Applied Chemistry, Chinese Academy of Sciences successfully constructed a new type of nanotheranostic agent (UCNPs@mSiO$_2$@DOX-ZnO) with UCNPs as the core for bio-imaging, and a mesoporous silica layer as the outer shell with ZnO as "gatekeeper" for pH-triggered drug delivery (Figure 1) [1]. The UCNPs inner core is not only responsible for upconversion luminesce (UCL) imaging, but also used as contrast agent for computed tomography (CT) and magnetic resonance imaging (MRI) owing to the magnetic property and strong X-ray attenuation of Gd and Yb. The bio-imaging experiments firmly demonstrate that the UCNPs@mSiO$_2$-ZnO effectively serve as contrast agents for UCL/CT/MRI tri-modality imaging both *in vitro* and *in vivo*. Taking advantage of different modality imaging together, it provides much more detailed and exact information for cancer diagnosis than single-modality imaging. The authors choose the biodegradable ZnO nanoparticles as "gatekeeper" to control the drug release since they are highly responsive to acids. They can efficiently block the drug in the mesopores for preventing the premature drug release until it is dissolved in the acidic environment around tumors to realize sustained release of the drug. The tests of intracellular drug release further confirm that the acid metabolized by tumors could easily open the "gate" guarded by ZnO to achieve pH-triggered on-demand drug release. More importantly, ZnO is non-toxic against normal tissues, but exhibits cytotoxic effects after dissolution, resulting in a higher therapeutic effectiveness of the nanotheranostic agent for cancer but very low side effects.



Fiugre 1 Synthesis of UCNPs@mSiO$_2$@DOX-ZnO for multi-modality imaging guided pH-triggered chemotherapy.

Zhang and co-authors have constructed a novel nanoplatform based on UCNPs for multi-modality bio-imaging and pH-triggered on-demand drug release. The developed strategy is expected to provide an effective and universal method to construct other imaging-guided on-demand chemotherapies in cancer treatment, helping to enhance therapeutic efficacy and reduce side effect.

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1 Wang YH, Song SY, Liu JH, Liu DP, Zhang HJ. ZnO-functionalized upconverting nanotheranostic agent: multi-modality imaging-guided chemotherapy with on-demand drug. *Angew Chem Int Ed*, 2015, 54: 536–540