Near-infrared semiconducting polymer brush and pH/GSH-responsive polyoxometalate cluster hybrid platform for enhanced tumor-specific phototheranostics

With the support by the National Natural Science Foundation of China, a research team directed by Prof. Wang Wei (王维) at the Institute for Cell Transplantation and Gene Therapy, Third Xiangya Hospital of Central South University, recently reported a novel tumor microenvironment (TME)-responsive phototheranostic paradigm (SPB@POM), which was published in *Angewandte Chemie International Edition* (2018, 57: 14101—14105.).

Having highly polarizable π-systems, the near-infrared (NIR)-absorbing organic semiconducting polymers (SPs) are an outstanding phototheranostic paradigm for photoacoustic (PA) imaging and photothermal therapy (PTT) of carcinoma. However, some inherent issues remain that hinder their practical applications in the clinic. For example, the conventional water-soluble SP nanoparticles (SPNs) fabricated by nano-coprecipitation exhibit poor stability under physiological conditions. Another problem is that the SPNs are usually taken up by tumor-adjacent tissues owing to the relatively low passive targeting efficiency, which is a significant cause of off-target hyperthermia of noncancerous regions during photothermal therapy (PTT).

Wang's group developed an intelligent pH/GSH dual-responsive hybrid nanoplatform (SPB@POM) based on the combination of inorganic POM (polyoxometalate clusters) and organic SP brush for concurrent tumor-specific self-assembly and phototheranostic enhancement. The well-designed SPB@POM was capable of acidic TME-driven self-aggregation and reducing TME-triggered NIR absorption enhancement, thus resulting in improved PA imaging contrast and PTT efficacy. The hybrid of SPBs and POM clusters not only resolved the rapid metabolism of ultra-small POMs in blood but also greatly decreased the dosage of SP, thus achieving an unprecedented phototheranostic efficacy.

These findings may provide guidance in the future design of tumor-specific phototheranostic nanoplatforms for precise cancer therapy.

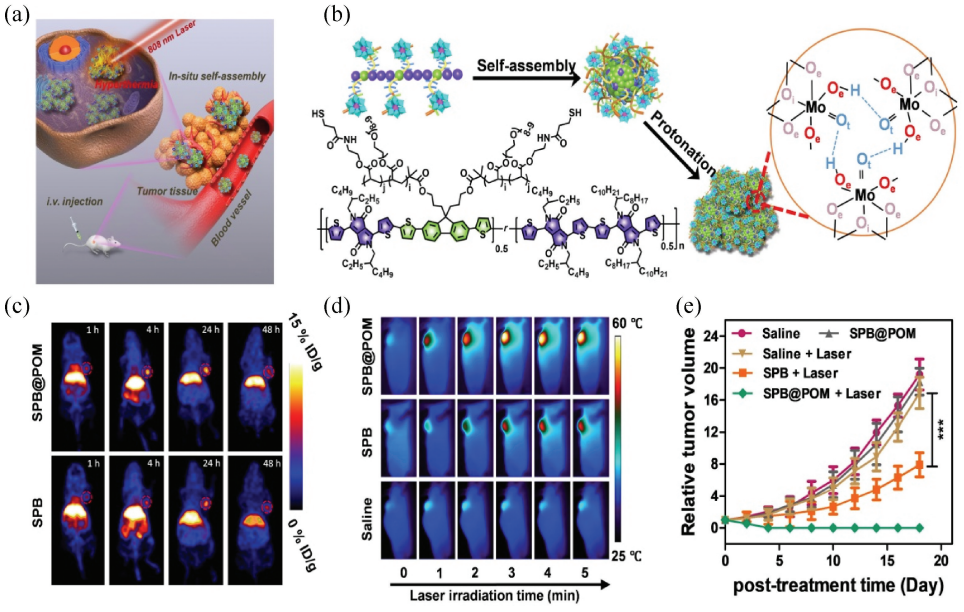

Figure (a) Schematic of acidic/reductive TME-responsive SPB@POM for tumor-specific self-assembly and phototheranostic enhancement. (b) Structure of SPB, synthesis of SPB@POM and mechanism of acidity-induced aggregation of SPB@POM. (c) The PET imaging of U87MG tumor-bearing mice by *i. v.* injection of SPB and SPB@POM. (d) IR thermal imaging of U87MG tumor-bearing mice during 5 min of 808 nm laser irradiation after *i. v.* injection of SPB, SPB@POM and saline. (e) Tumor growth curves of U87MG tumor-bearing mice subjected to varied treatments. $*P<0.05$; $**P<0.01$; $***P<0.001$.