

## Supporting Information

### **Self-assembled inorganic/organic hybrid nanoparticles with multi-functionalized surfaces for active targeting drug delivery**

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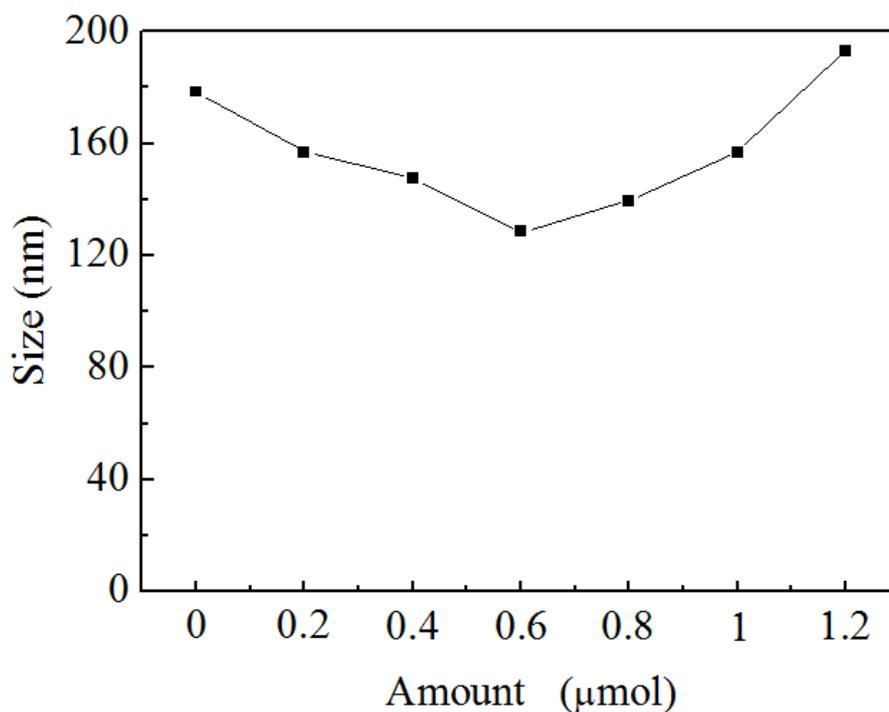


Figure S1. Effect of  $\text{Ca}^{2+}$  and  $\text{CO}_3^{2-}$  amounts on the size of nanoparticles composed of HP, CTS and  $\text{CaCO}_3$ .

During the preparation of hybrid nanoparticles, we adjusted amount of  $\text{Ca}^{2+}$  and  $\text{CO}_3^{2-}$  ions to study the effect of  $\text{CaCO}_3$  content on the nanoparticle size. As shown in Figure S1, the nanoparticle size exhibited a biphasic dependence on the amounts of to the  $\text{Ca}^{2+}$  and  $\text{CO}_3^{2-}$  ions. With the absence of  $\text{Ca}^{2+}$  and  $\text{CO}_3^{2-}$  ions, the size of the formed nanoparticles composed by HP and CTS was 178 nm. With the increase in the amounts of the  $\text{Ca}^{2+}$  and  $\text{CO}_3^{2-}$  ions in the self-assembly system, a gradual decrease followed by an increase in the particle size were observed. The minimum size was obtained when the amount of  $\text{Ca}^{2+}$  ion was 0.6  $\mu\text{mol}$  and the amount of  $\text{CO}_3^{2-}$  ions was 0.6  $\mu\text{mol}$ .

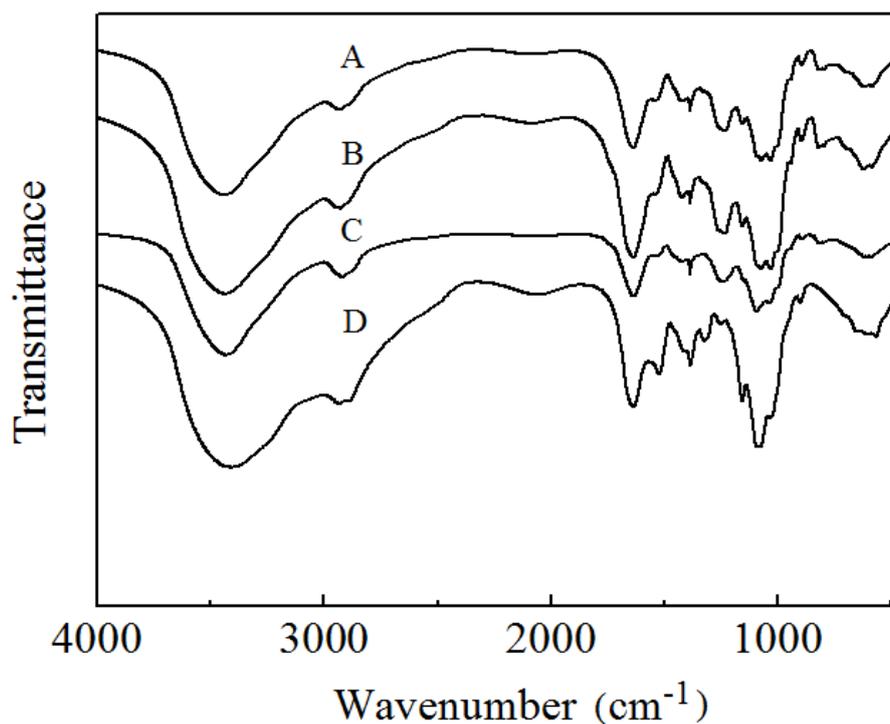


Figure S2. FTIR spectra of HP/CTS nanoparticles (A), HP/CTS/CaCO<sub>3</sub> nanoparticles, (B), HPB/HP/CTS/CaCO<sub>3</sub> nanoparticles (C), and CTS (D).

As shown in Figure S2, from the spectra of HP/CTS, HP/CTS/CaCO<sub>3</sub>, HPB/HP/CTS/CaCO<sub>3</sub> nanoparticles, both characteristic bands from chitosan (amine groups at 1540 cm<sup>-1</sup>) and heparin (-OSO<sub>3</sub> groups at 1220 cm<sup>-1</sup>) could be observed. For HP/CTS/CaCO<sub>3</sub>, HPB/HP/CTS/CaCO<sub>3</sub> nanoparticles, no obvious peaks from CaCO<sub>3</sub> in the hybrid nanoparticles could be observed because of the low amount of CaCO<sub>3</sub> in those hybrid nanoparticles.

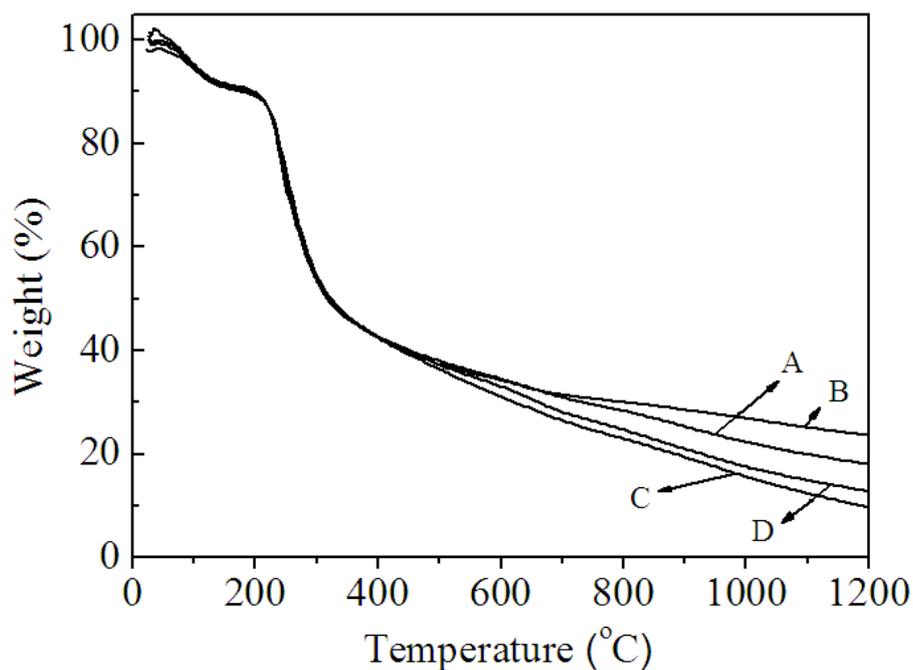


Figure S3. TGA curves of (A) HP/CTS nanoparticles, (B) HP/CTS/CaCO<sub>3</sub> nanoparticles, (C) DOX loaded HP/CTS nanoparticles, and (D) DOX loaded HP/CTS/CaCO<sub>3</sub> nanoparticles.

TGA was used to characterize the thermal property of both blank hybrid nanoparticles and DOX loaded hybrid nanoparticles. As seen in Figure S3, Compared with the blank nanoparticles, DOX loaded nanoparticles showed slightly higher weight loss values due to the drug loaded inside the nanoparticles.

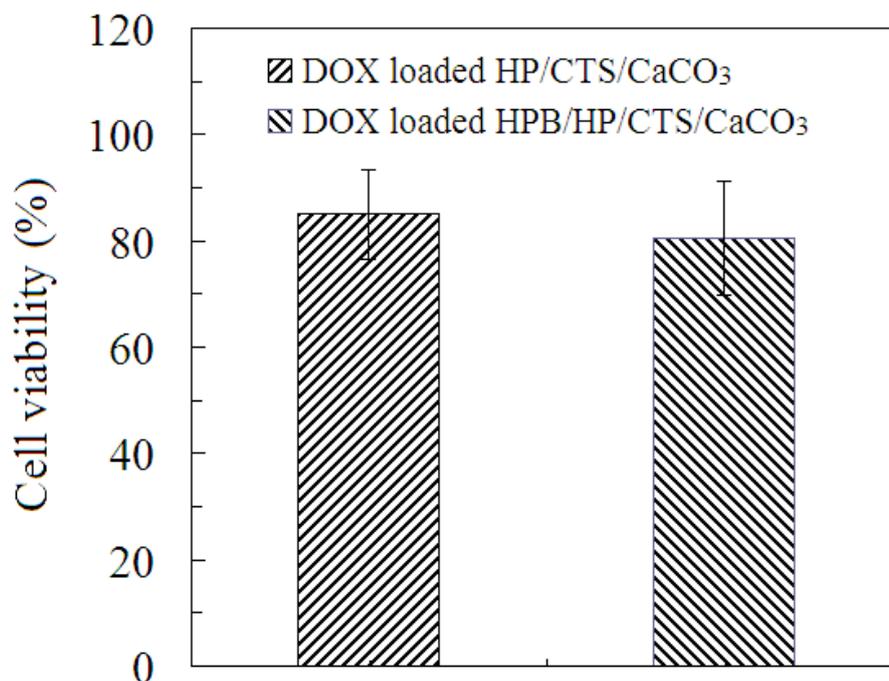


Figure S4. Cell viability of HEK 293T cells after treated by DOX loaded nanoparticles.

HEK 293T cells without overexpression of biotin receptor were treated by the nanoparticles without biotin moiety (DOX loaded HP/CTS/CaCO<sub>3</sub>) and the nanoparticles with biotin moiety (DOX loaded HPB/HP/CTS/CaCO<sub>3</sub>). As shown in Figure S4, there was no apparent difference in cell viabilities for the cells treated by DOX loaded HP/CTS/CaCO<sub>3</sub> and DOX loaded HPB/HP/CTS/CaCO<sub>3</sub> because HEK 293T cells were not biotin receptor overexpressed cells.