Supplementary Information

Experimental details

Reagents and materials: Chloroauric acid ($HAuCl_4$) was purchased from Shanghai Chemical Reagent Company (Shanghai, China). Sodium borohydride and cysteamine were purchased from Sinopharm Chemical Reagent Company (Beijing, China). Heparin sodium salt was obtained from Aladdin Chemistry Co. Ltd (185 U/mg, Shanghai, China). Heparin stock solution (1.00 mg/mL) was prepared by dissolving 0.1000 g of heparin sodium reagent in water and diluting to the mark in a 100 mL calibrated flask. The working solution was further diluted with water. All other solvents and reagents in this investigation were of analytical grade and used without further purification. Millipore water (18 MΩ cm) was used in all experiments. The experiments were conducted at room temperature (ca. 20 °C).

Apparatus: UV-visible adsorption spectra were recorded on a U-3900H UV-Vis Spectrophotometer (Hitachi, Japan) at room temperature using a 500 μL black-body quartz curette with 1 cm path length. The photographs were taken with a Cannon 500 digital camera. The pH measurements were carried out on model PB-10 digital ion analyzer (Sartorius Scientific instruments Co., Ltd., China, Beijing). Transmission electron microscopy (TEM) measurements were made on a JEM-2100 transmission electron microscope (Jeol Co. Ltd, Japan). The samples for TEM characterization

were prepared by placing a drop of colloidal solution on carbon-coated copper grid and dried at room temperature. Zeta potentials were recorded with a Nano ZS Laser Scattering Particles Size Analyzer (Malvern, England).

Preparation of positively-charged AuNPs: All glassware used in the following procedure was cleaned in a bath of freshly prepared 3:1 HNO_3–HCl, rinsed thoroughly in water and dried in air prior to use. The positively-charged AuNPs were prepared according to the published protocol.[1] Briefly, a cysteamine solution (400 μL, 213 mM) was added to 40 mL of 1.42 mM $HAuCl_4$ solution. After stirring for 20 min at room temperature, 10 μL of 10 mM $NaBH_4$ solution was added, and the mixture was vigorously stirred for 10 min at room temperature in the dark. Then, the mixture was further stirred 15 min, and the resulting win-red solution was stored in the refrigerator (4 °C) and ready for use. The as-prepared AuNPs were charactered with UV-Visible absorption spectra and TEM. The results of TEM showed that the average size of the AuNPs was about 34 nm. The concentration of the AuNPs solution was 10.5 nM, which was estimated by the original concentration of the gold solution.[2]

Colorimetric detection of heparin: The heparin-induced aggregation of AuNPs was monitored by observing the UV-Vis spectral change during the addition of heparin to colloidal AuNPs. In a typical procedure, 30 μL

aqueous heparin solution (with appropriate concentration) was added to the colloidal AuNPs (180 μL), and the solution was diluted with buffer solution to 500 μL, then the solution was allowed to react for 15 min at room temperature. Absorption spectra of the reacted solution were collected in the range of 400–800 nm at room temperature. The concentration of heparin was quantified by the absorption ratio (A_{670}/A_{520}). All the measurement of heparin has been performed in pH 3.6 Britton-Robinson (B-R) buffer solution (0.04 M).

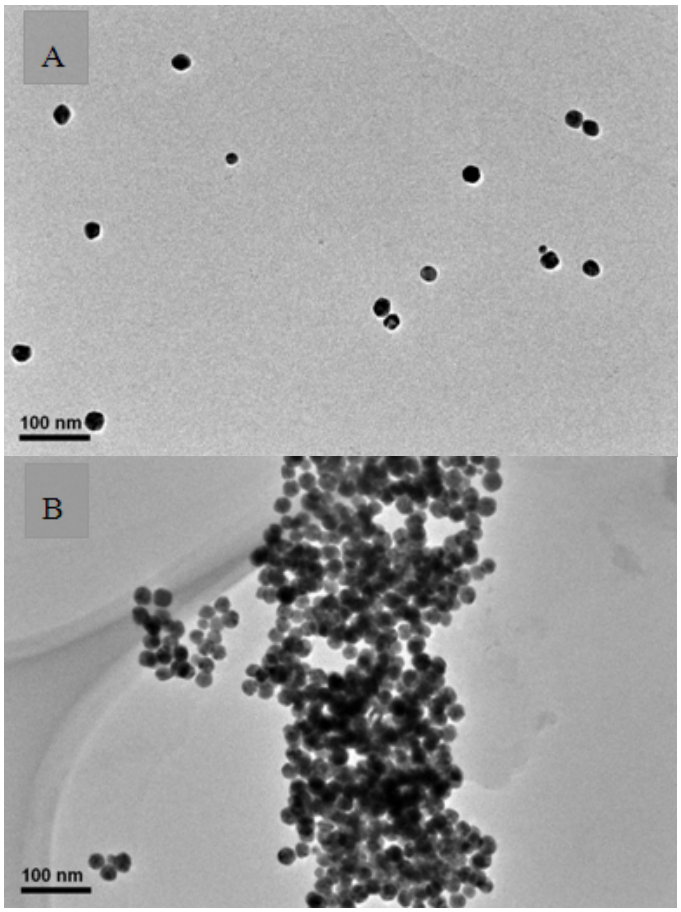

Figure S1 TEM images of AuNPs (~34 nm) (A) in the absence of heparin, and (b) in the presence of 5 μg/mL heparin.

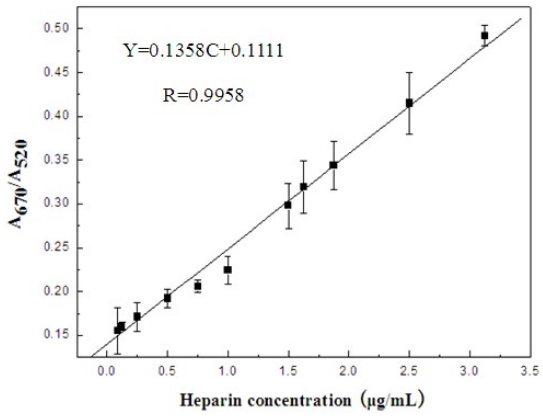

Figure S2 Plots of the absorption ratio (A_{670}/A_{520}) vs. heparin concentration. Experimental condition: 200 μL B-R buffer (pH 3.6), 180 μL AuNPs, 15 min incubation time, and room temperature.

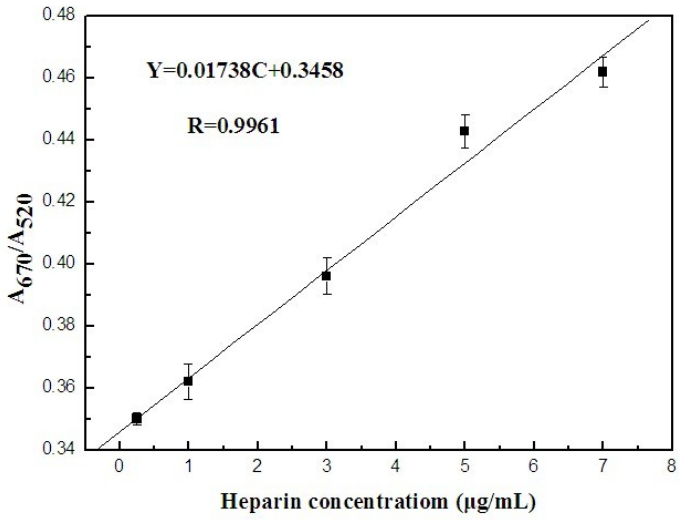

Figure S3 Plots of the absorption ration (A_{670}/A_{520}) *vs*. heparin concentration in 1% serum. Experimental condition: 200 μL B-R buffer (pH 3.6), 180 μL AuNPs, 15 min incubation time, and room temperature.

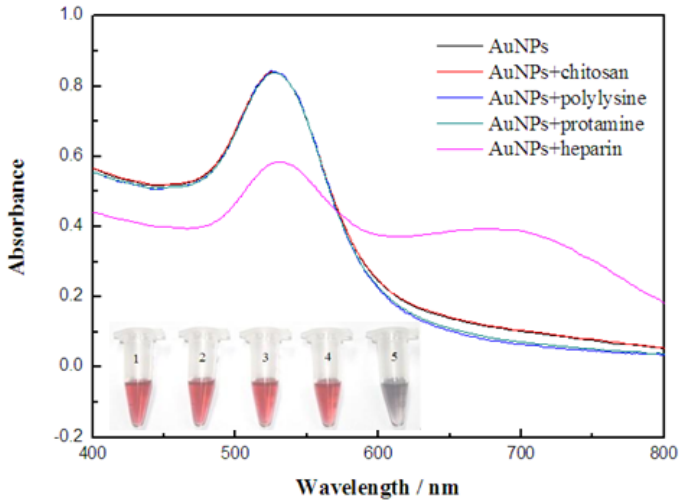

Figure S4 Absorption spectra of (1) AuNPs alone, (2) AuNPs + 3 μg/mL chitosan, (4) AuNPs + 3 μg/mL polysin, (4) AuNPs + 3 μg/mL protamin and (5) AuNPs + 3 μg/mL heparin. Inset shows the corresponding photographs of AuNPs solutions. Experimental conditions: 200 μL B-R buffer (pH 3.6), 180 μL AuNPs, and room temperature.

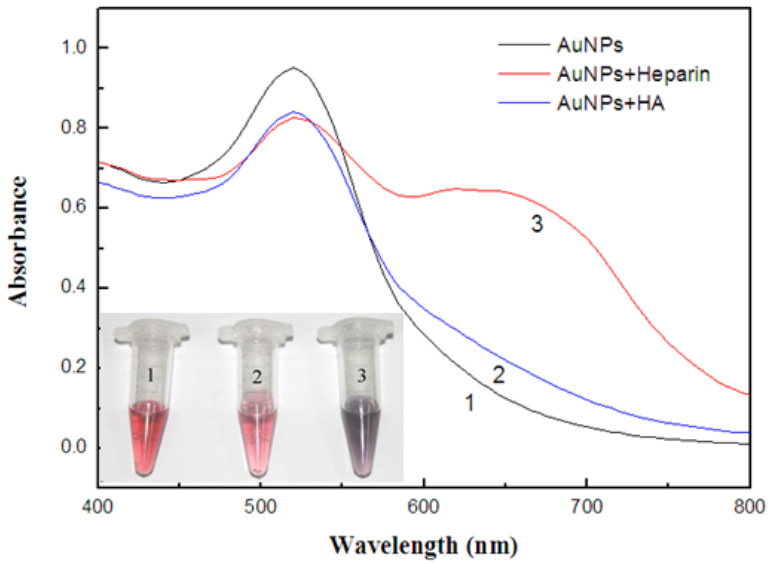

Figure S5 Absorption spectra of (1) AuNPs alone, (2) AuNPs + 3 μg/mL HA, and (3) AuNPs + 3 μg/mL heparin. Inset shows the corresponding photographs of AuNPs solutions. Experimental conditions: 200 μL B-R buffer (pH 3.6), 180 μL AuNPs, and room temperature.

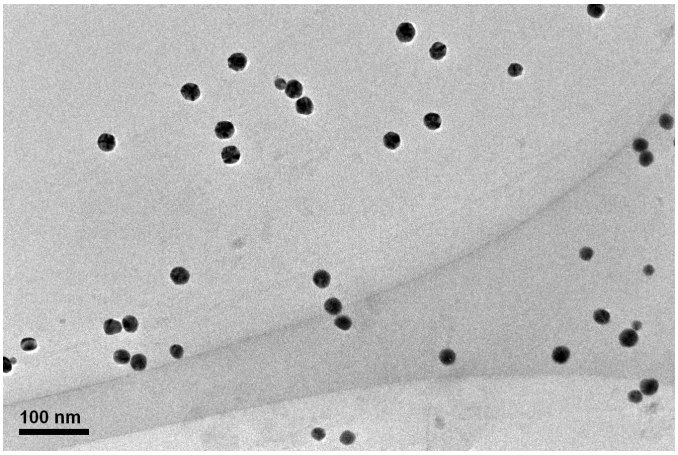

Figure S6 TEM image of AuNPs + 3 μg/mL HA

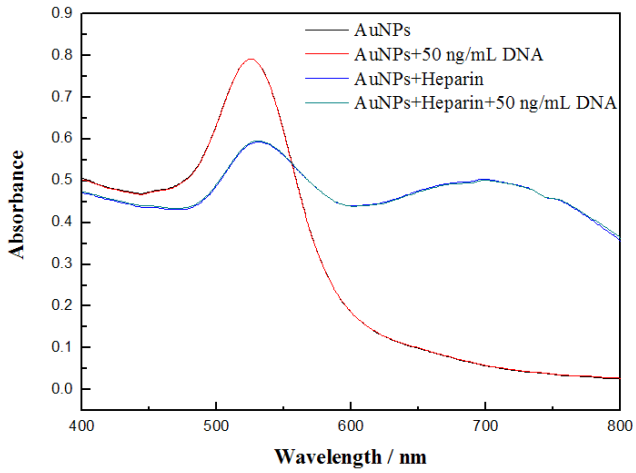

Figure S7 Absorption spectra of AuNPs alone (black), AuNPs + 50 ng/mL DNA (red), AuNPs + 3 μg/mL heparin (blue), and AuNPs + 3 μg/mL heparin + 50 ng/mL DNA (green). Experimental conditions: 200 μL B-R buffer (pH 3.6), 180 μL AuNPs, and room temperature.

References

1 T. Niidome, K. Nakashima, H. Takahashi and Y. Niidome, *Chem. Commun.,* 2004, 1978–1979.

2 Neiman, B.; Grushka, E.; Lev, O. *Anal. Chem.,* 2001, **73**, 5220–5227.