

ELECTRONIC SUPPLEMENTARY INFORMATION (ESI)

DNA-Caged Gold Nanoparticles for Controlled Release of Doxorubicin by a DNA Enzyme and pH

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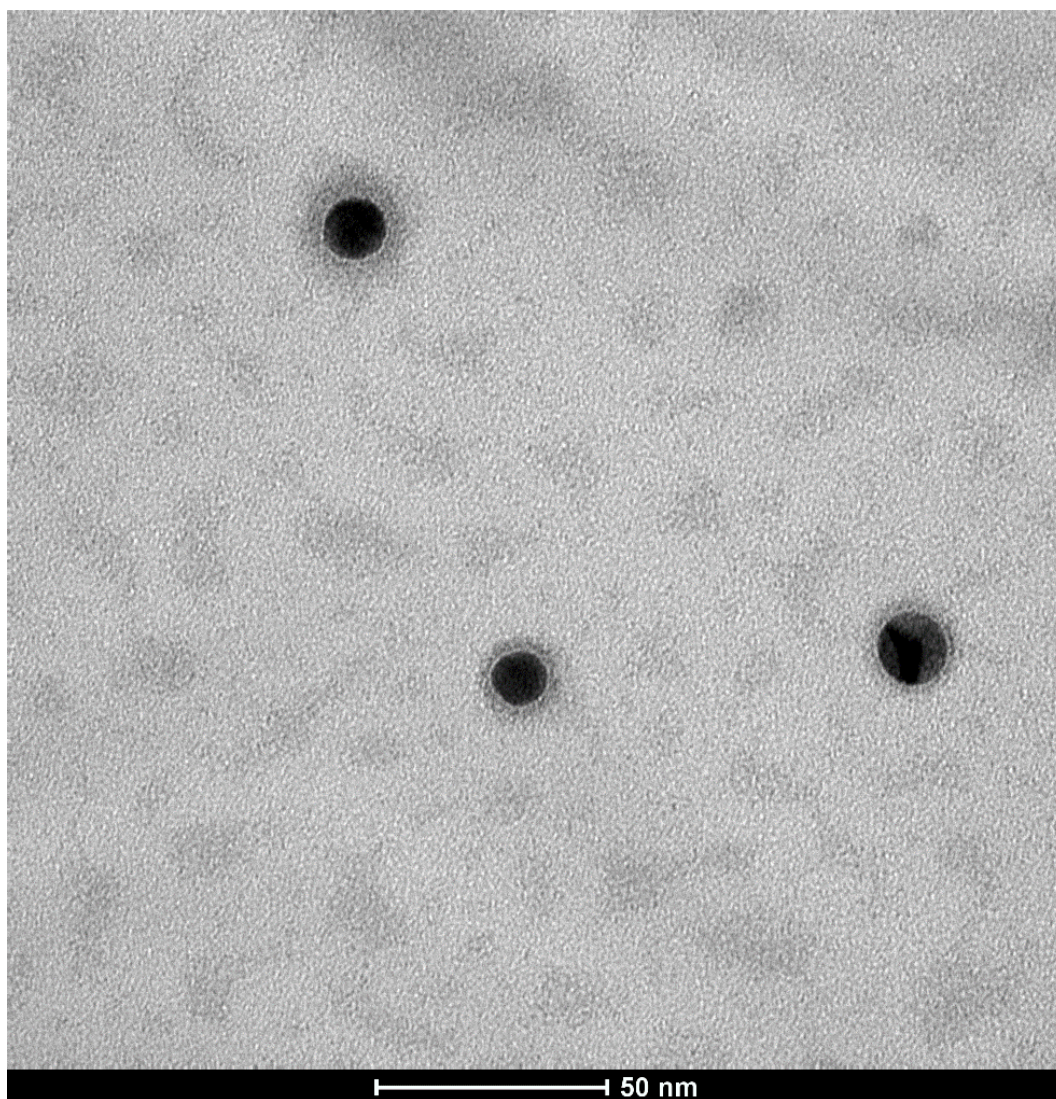


Figure S1A. More TEM images of ds DNA polyhedron caged AuNPs. The halos can be seen clearly around each AuNPs.

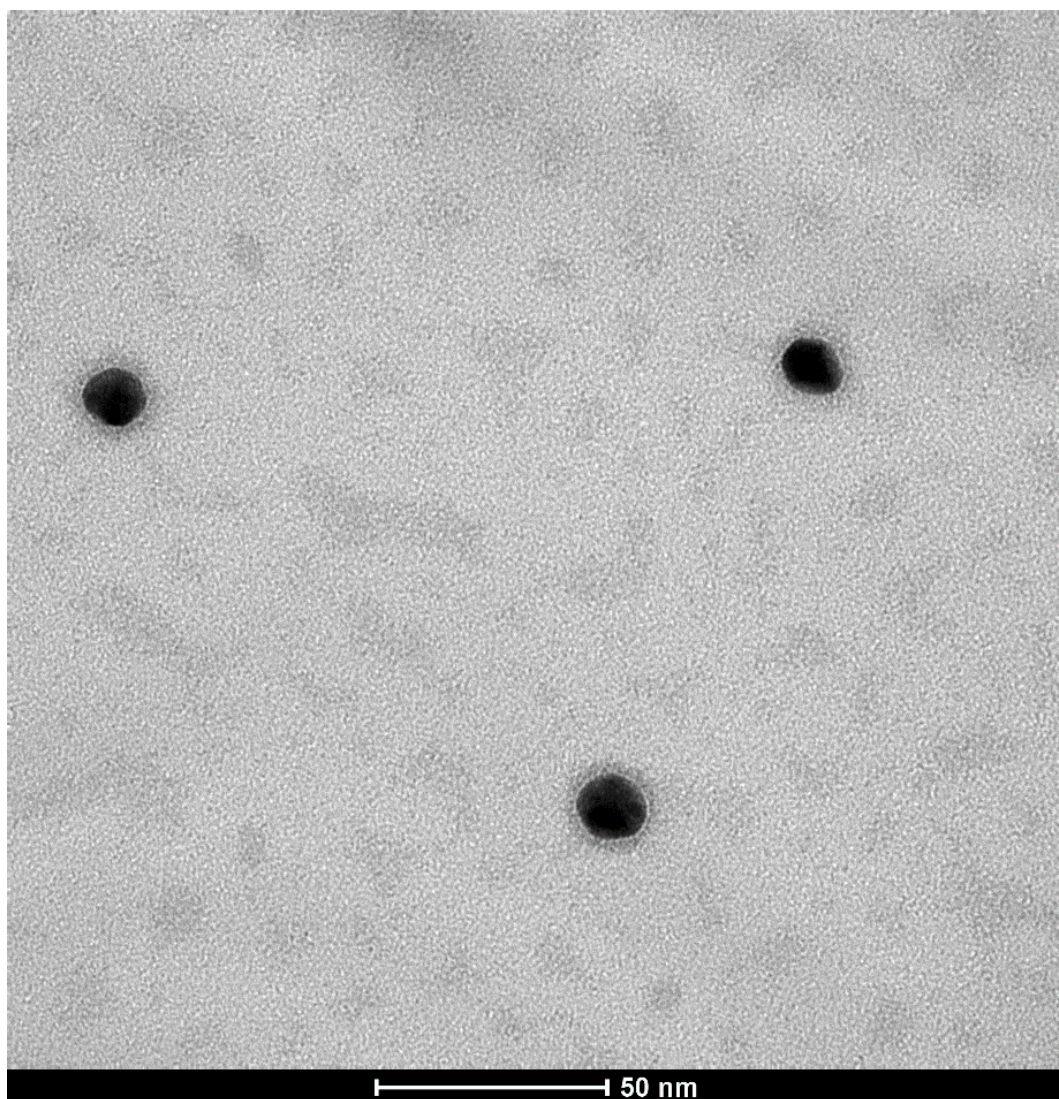


Figure S1B. More TEM images of ds DNA polyhedron caged AuNPs. The halos can be seen clearly around each AuNPs.

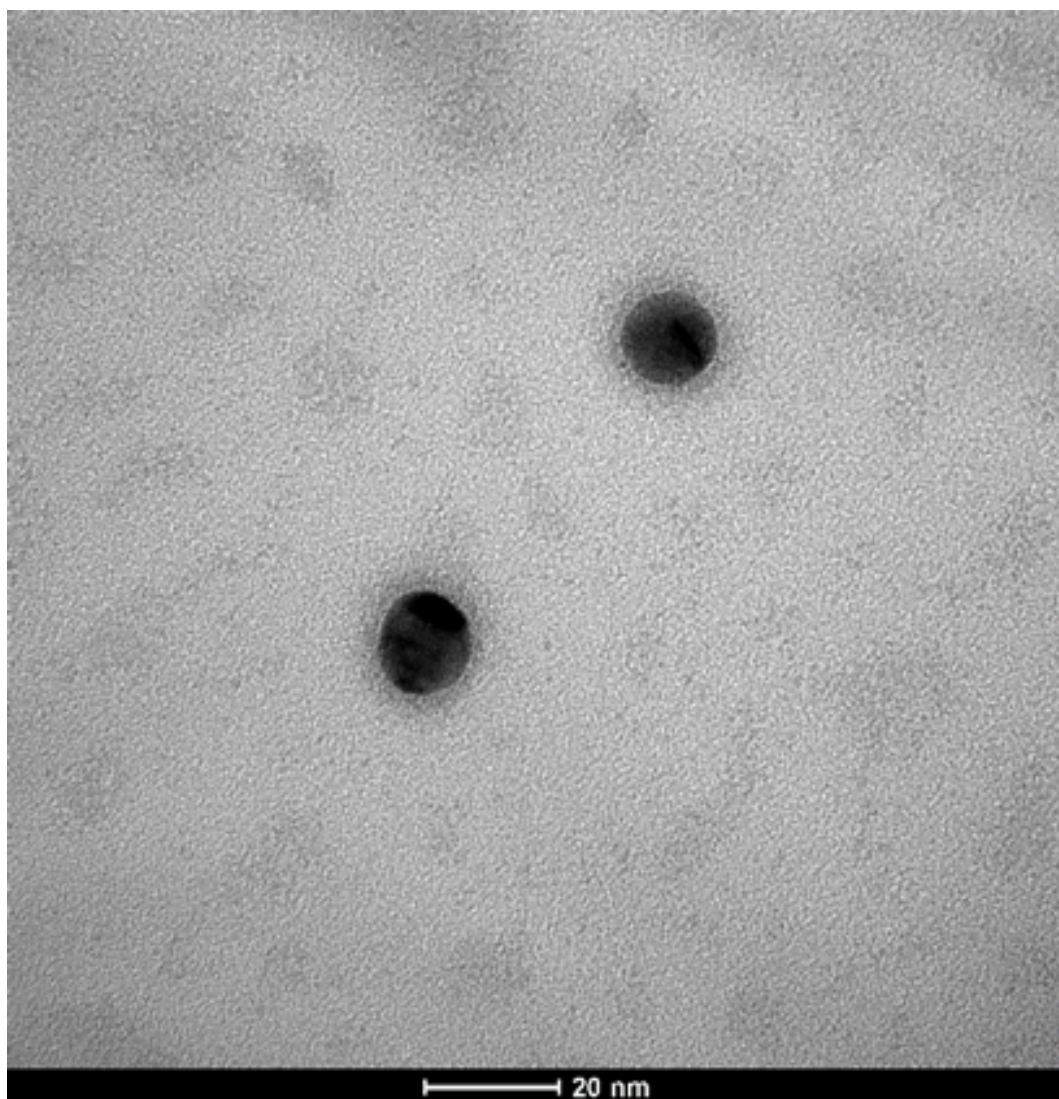


Figure S1C. More TEM images of ds DNA polyhedron caged AuNPs. The halos can be seen clearly around each AuNPs.

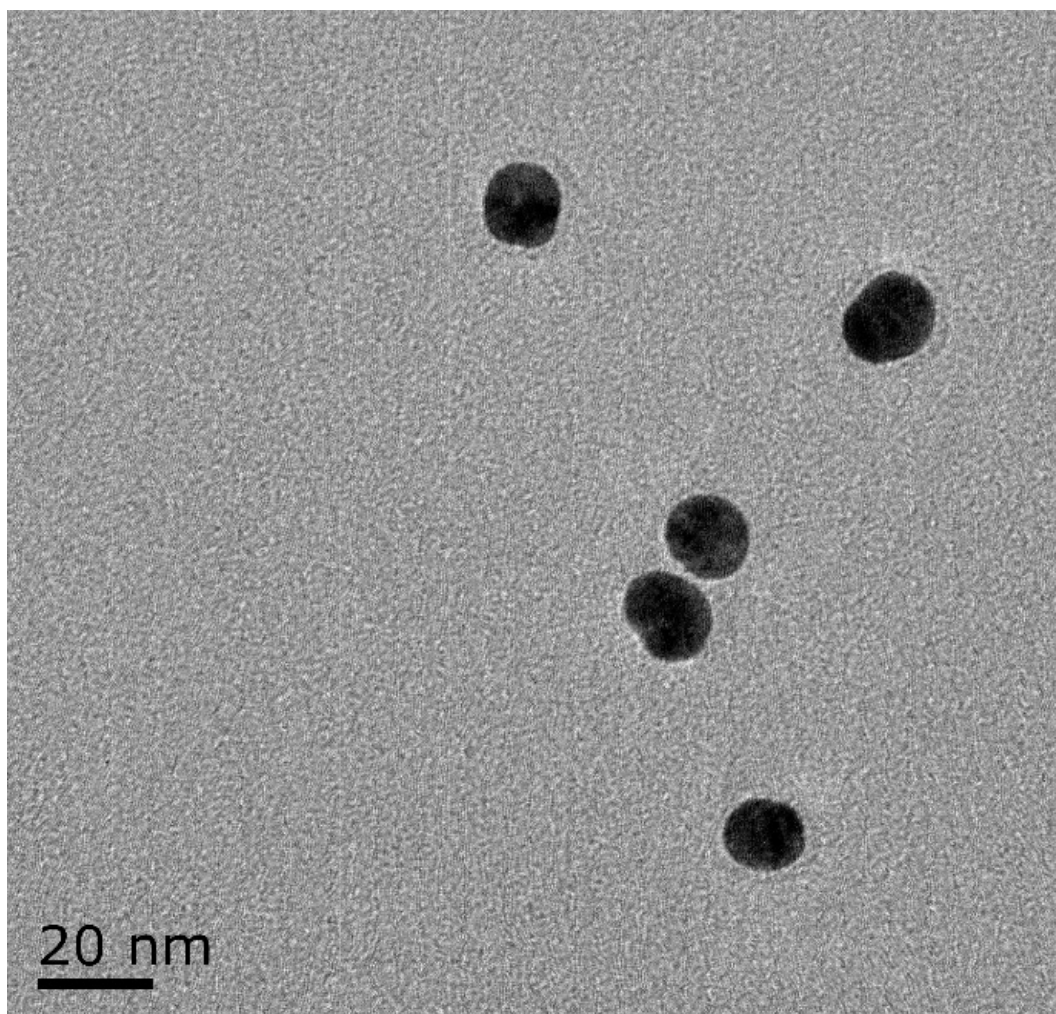


Figure S1D. More TEM images of ds DNA polyhedron caged AuNPs. The halos can be seen clearly around each AuNPs.

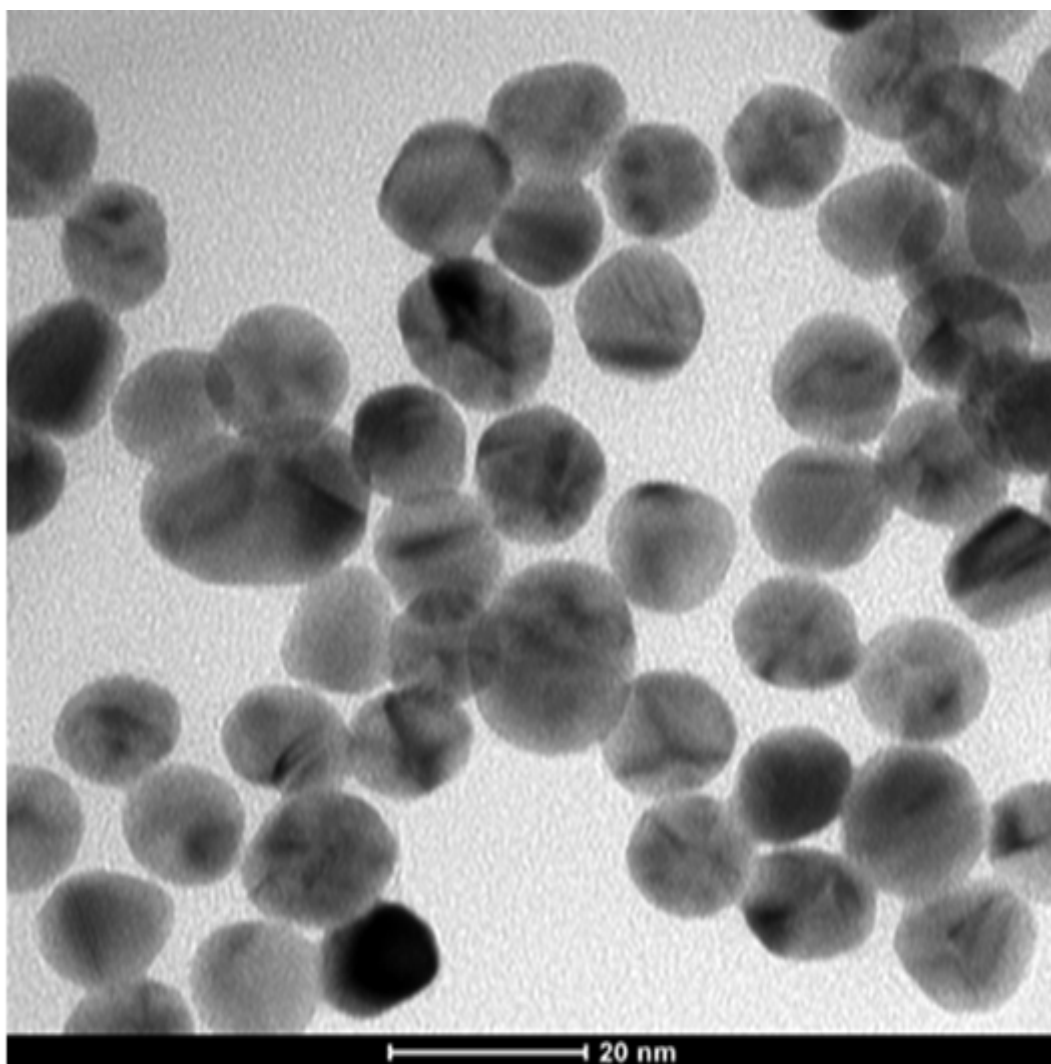


Figure S2. The TEM images of the original AuNPs. No halos can be seen around the original AuNPs.

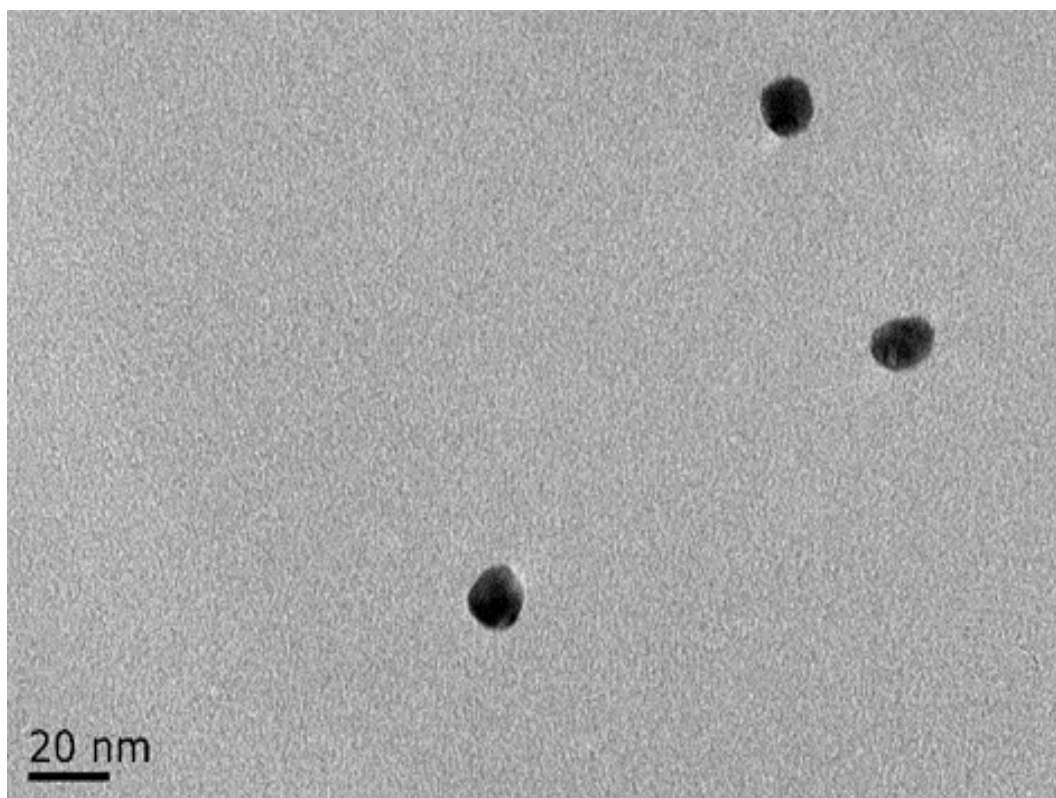


Figure S3. The TEM pictures of the nanoparticles only functionalized by ss DNA. No halos can be seen around the ss DNA functionalized AuNPs.

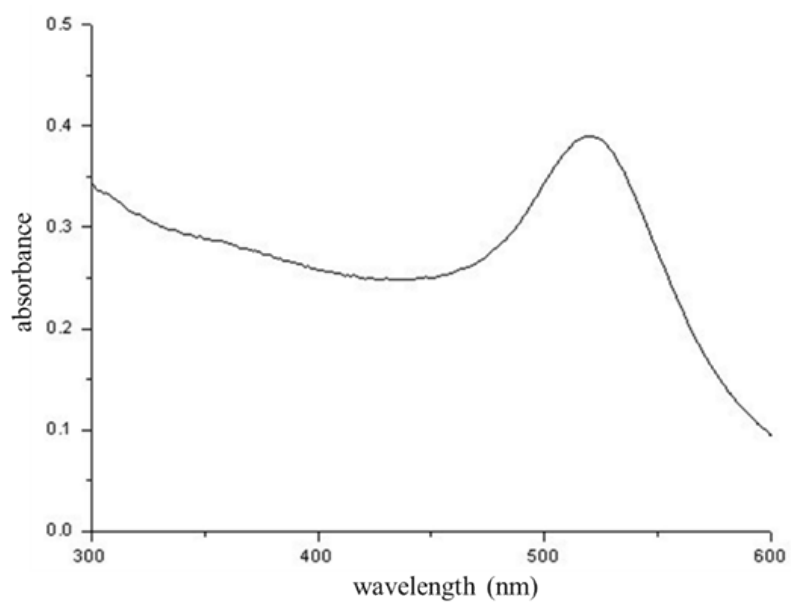


Figure S4. The UV-Vis-NIR spectrum of AuNP shows the maximum absorption peak is at 520 nm.

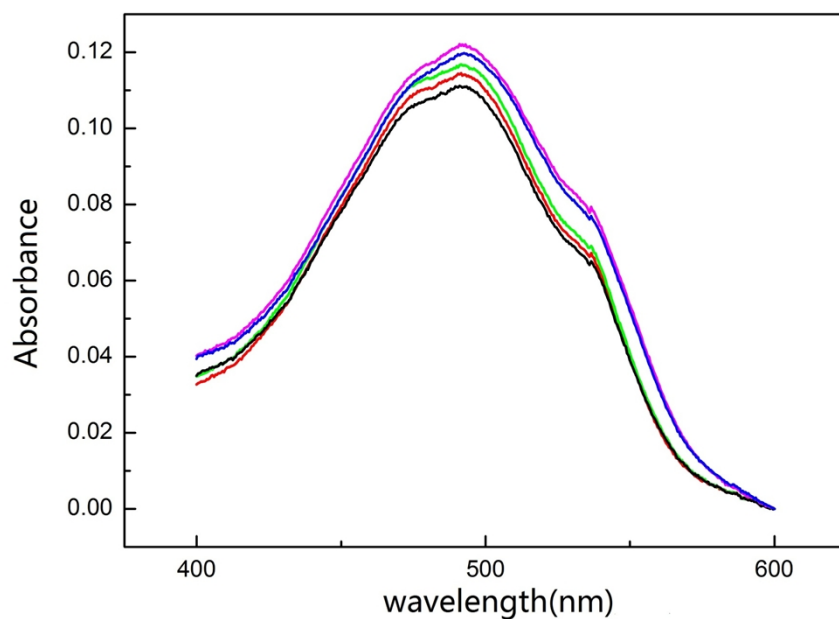


Figure S5. The control experiments are determined by the ultraviolet spectrum, Doxorubicin release curve from the AuNPs-nanocages systems doesn't shows the markedly increasing of absorption of doxorubicin at 490nm.

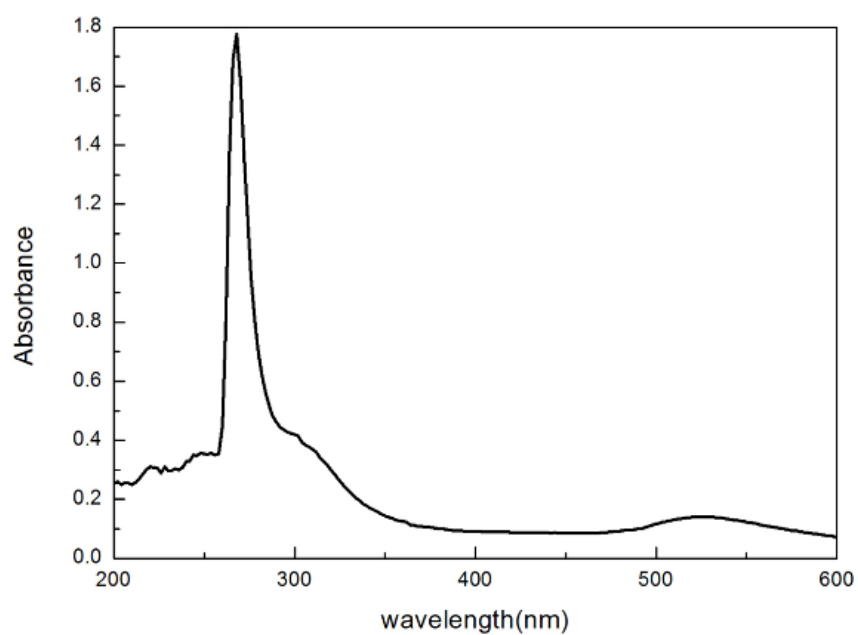


Figure S6. The UV-Vis-NIR spectra of the supernatant of DNA-AuNPs complex solution exposed to the 520nm laser. The absorption peak of DNA is 280nm, so it is clear that lots of DNA exist in the supernatant

EXPERIMENTAL SECTION

Oligonucleotides.

DNA sequences are as follows. DNA attached to nanoparticles: 5' TGGATCATCGACTGTGCCTTCTA 3', these strands were modified by sulfhydryl at the 5' end.

Strand I: 5' ATAGTGAGTCGTATTAATTAACCCTCACTAAAAAGGATCCGGATCCTT3'

Strand II: 5' TTTAGTGAGGGTTAATCATACGATTTAGGTGAAAGGATCCGGATCCTT3'

Strand III: 5' TCACCTAAATCGTATGGGAGCTCTGCTTATATAAGGATCCGGATCCTT3'

Strand IV: 5' ATATAAGCAGAGCTCCTAATACGACTCACTATTAGAAGGCACAGTCGA3'

Reagents. All oligonucleotides were obtained from Shanghai Sangon biotechnology Co., Ltd. (Shanghai China) and used as obtained. All Primer oligonucleotides were design by the software Primer Premier. The sequence of synthesized oligonucleotides is given in Table S1. Trisodium citrate, HAuCl_4 , NaH_2PO_4 , Na_2HPO_4 , and NaCl were of analytical grade and purchased from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). Tween-20 was obtained from Sunshine biotechnology (Nanjing China) Co., Ltd. Tris-(2-carboxyethyl) phosphine hydrochloride (TCEP) was provided by Thermo Scientific (USA). Double distilled water was used for all of the experiments.

Preparation of Citrate-capped AuNPs. 5 mL of 38.8 mM Trisodium citrate was added rapidly into a stirred boiling aqueous solution containing 50 ml of 1 mM HAuCl_4 . The solution turned into clear, black, purple and deep red in sequence within 2 min. After the solution was kept boiling and stirred for 15 min, it was naturally

cooled down to room temperature. The final colloidal solution was stored at 4 °C for further used. The concentration of AuNPs was 13 nM calculated by lambert-beer law. The extinction coefficient of $2.7 \times 10^8 \text{ M}^{-1} \text{ cm}^{-1}$ at 520 nm for 13 nm AuNPs was used in this work.

Preparation of DNA-functionalized AuNPs. To activate the thiol-DNA, 20 μL of 100 μM DNA was added to 5 μL of 20 mM Tris buffer (pH 7.3) containing 100 mM TCEP. The resultant solution was incubated for 1 h at room temperature. After incubation, the activated oligonucleotides were purified using Millipore's Amicon Ultra-0.5 centrifugal filter device to remove excess TCEP. The freshly deprotected and purified DNA was later added to 500 μL of gold colloidal solution to functionalize the AuNPs. The mixed solution was sonicated for 10 s, and then incubated for 20 min with shaking at room temperature. After that, the resultant solution was mixed with 0.1 M phosphate buffer (pH 7.2) containing 0.1% sodium dodecyl sulfate (SDS) and the final concentration of phosphate and SDS was brought to 0.01 M and 0.01%, respectively. The solution was sonicated for 10 s, and incubated for 20 min. In the subsequent salt aging process, the concentration of NaCl first increased to 0.05 M using 2 M NaCl. The process was repeated at one more increment of 0.05 M NaCl and for every 0.1 M NaCl increment thereafter until a concentration of 0.5 M NaCl was reached. After each addition of NaCl, the DNA-AuNPs were vortexed, sonicated for 10s, and then incubated for 20 min. After the salt aging, the mixture was shaken at room temperature overnight. To remove excess DNA, the solution was centrifuged at 13,200 rpm for 20 min, and then redispersed in reaction

buffer (pH 8.0) containing 20 mM Tris, 200 mM NaCl, 5 mM MgCl₂, and 0.05% tween 20. Tween 20 was used to reduce the sticking of AuNPs to Eppendorf tube in this work. The step was repeated three times to sufficiently remove excess DNA. The good stability in salt aging process confirmed the successfully coupling of DNA to AuNPs

Formation of Icosahedral DNA-AuNPs Complexes. To assemble the Icosahedral DNA-AuNPs Complexes, 10 μ L 1000 nM for each strand of four groups of DNA (strands I, II, III, IV) were mixed with 60 μ L DNA-functionalized AuNPs in a Tris-Acetic-Mg²⁺ buffer that contained 40 mM Tris base (pH 8.0), 20 mM acetic acid, and 12.5 mM magnesium chloride. The samples were heated to 75 °C and then cooled to room temperature (24 °C). Although it took just 2.5 h for the samples to cool from 94 to 24 °C, 48 h were allotted to the cooling period. The assembled DNA samples were directly used for characterization, without further fractionation or purification. To remove excess DNA, the solution was centrifuged at 13,200 rpm for 20 min, and then redispersed in reaction buffer above (pH 8.0), the step was repeated three times to sufficiently remove excess DNA.

Doxorubicin Intercalation and release. For doxorubicin intercalation into DNA-AuNPs Complexes, 100 μ L doxorubicin (500 μ M) was mixed with 100 μ L DNA-AuNPs Complexes for 1 h and then centrifuged at 13,200 rpm at room temperature for 10 min. The amount of Doxorubicin released from the DNA-AuNPs Complexes was determined by measuring the ultraviolet absorption intensity of the supernatant using UV-vis spectroscopy (Shimadzu UV-2450). Solutions containing Doxorubicin

molecules were excited at 490 nm, and the emission intensities were measured in the range of 250-600 nm. According to the method, six tubes of samples were prepared. Then 10 μ L of T7 exonuclease enzyme (10U/ μ L) was added to each tube. Each sample was centrifuged after incubation for different time intervals and supernatant was extracted for next step measurement. The controlled release properties triggered by pH value were performed by incubating Doxorubicin-loaded DNA-AuNPs Complexes in 0.1 M phosphate buffer (pH 6.86) containing 20 mM phosphate, 200 mM NaCl, 5 mM MgCl₂. The release properties were then evaluated using the similar protocol as above.