Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.

Supporting Information

Surface-enhanced Raman Spectroscopy (SERS) Nanoprobes for Ratiometric Detection of Cancer Cells

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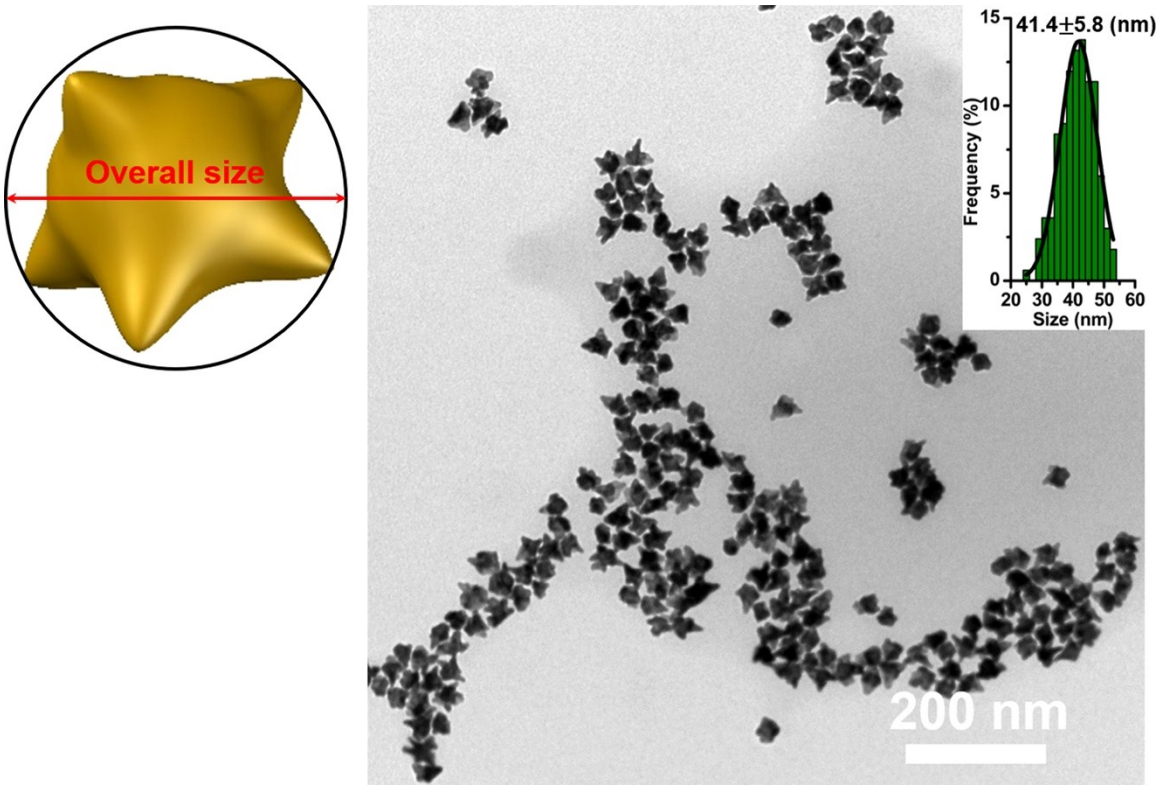

Figure S1. TEM image of gold nanostars used for preparation of SERS nanoprobes and size distribution statistically obtained from TEM image of GNSs using the ImageJ software. More than 150 GNSs were counted. The size of GNSs is called the overall size including the core and protruding tips, the model of which is schematically illustrated above. It can be seen that the overall size of GNSs is about 41.4±5.8 nm.

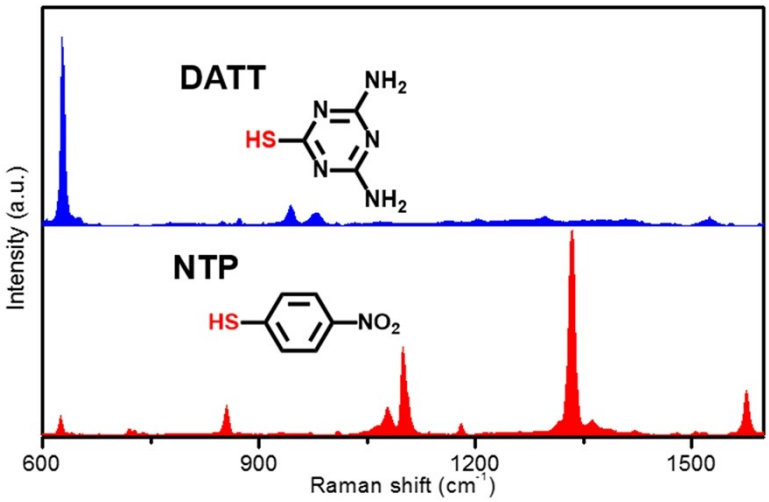

Figure S2. Spontaneous Raman spectra of NTP and DATT powder. The spectra were collected under the excitation of 785 nm with 5 mW power and 1 s integration time.

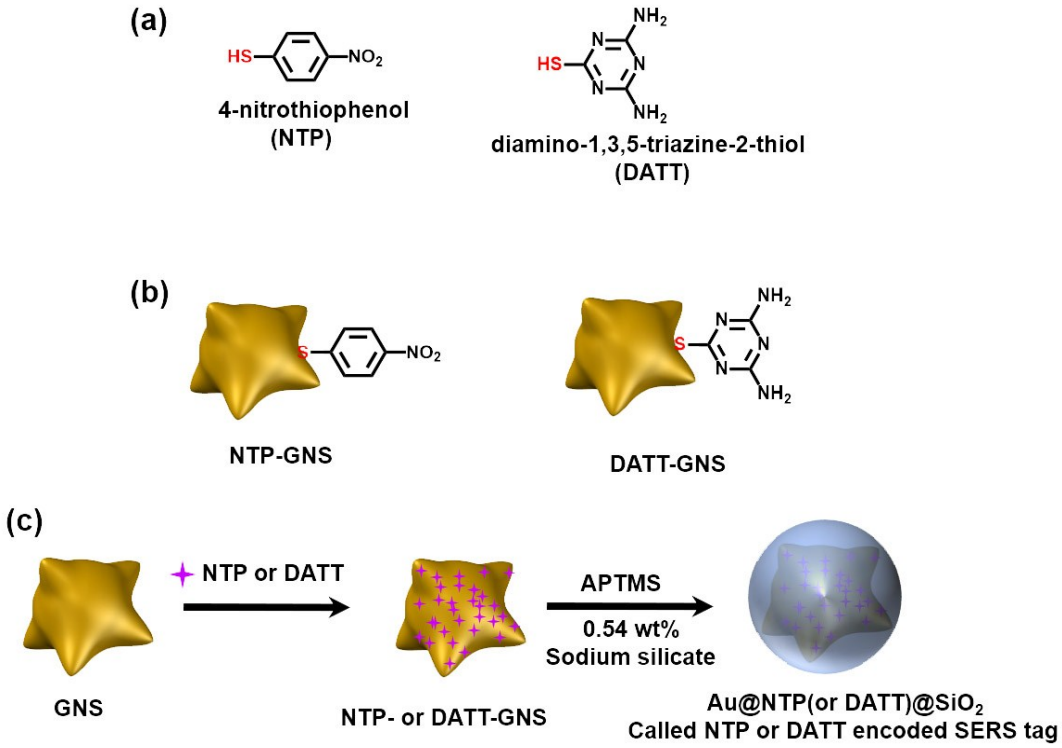

Figure S3. Schematic illustration of NTP or DATT encoded SERS tags. (a) Molecular structures of Raman reporters, 4-nitrothiophenol (NTP) and diamino-1,3,5-triazine-2-thiol (DATT), (b) Au-S interaction to form NTP (or DATT)-GNS complexes, and (c) synthesis progress of NTP or DATT encoded SERS tags. Raman reporters (NTP or DATT) are chemically bound onto the Au surface through the strong Au-S bond and then a SiO_2 layer are coated to encapsulate the encoded SERS tags, forming the sandwich structure, Au@Ramam-reporters@SiO_2. The SiO_2 layer possesses excellent biocompatible and can be used for flexible bioconjugation with biomolecules such as proteins, peptides and nucleic acids.

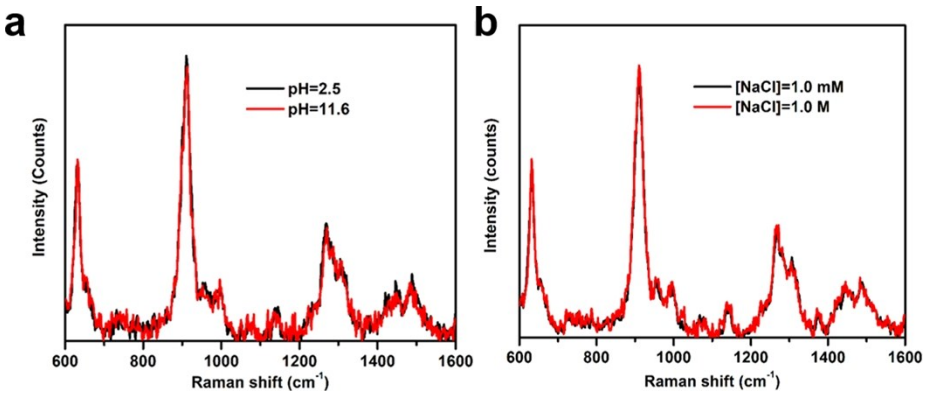

Figure S4. Stability of SERS nanoprobes without peptides conjugation. SERS spectra of SERS nanoprobes in the solution of (A) pH=2.5 and pH=11.6, (B) 1×PBS solution with 1.0 mM and 1.0 M NaCl. All results show that the present SERS nanoprobes have excellent stability against robust environments (e.g., pH, NaCl concentration).

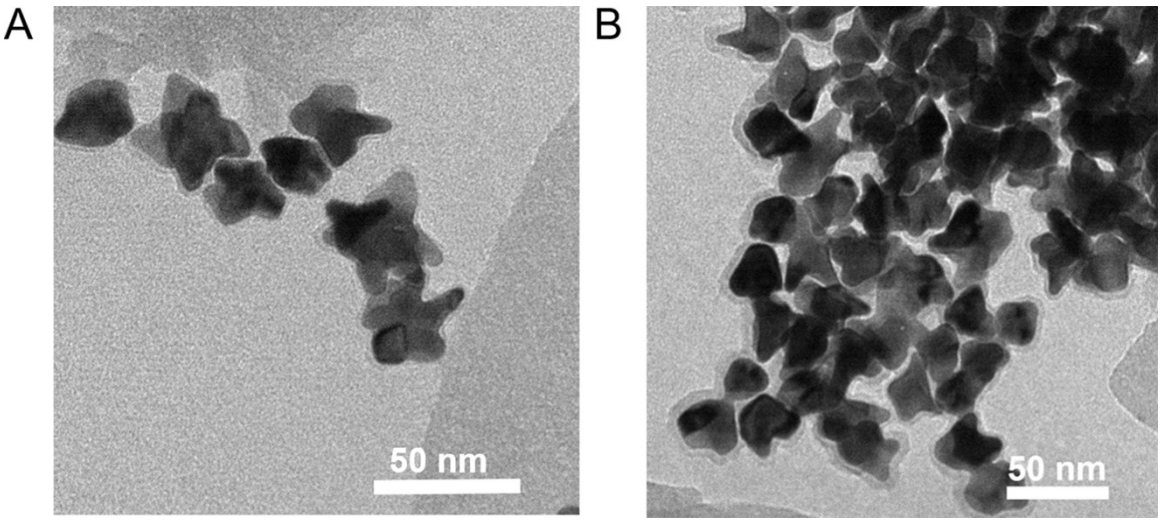

Figure S5. TEM image of (A) uPAR-SERS nanoprobes and (B) EGFR SERS nanoprobes. It can be seen that 3-5 nm silica layer was coated onto the GNS surface.

Table S1. Peak assignments of normal Raman bands and SERS bands of NTP, DATT, NTP-encoded SERS nanoprobes and DATT-encoded SERS nanoprobes [1-4]

NTP		NTP-encoded SERS nanoprobes		DATT		DATT-encoded SERS nanoprobes	
Peak (cm^{-1})	Assignment	Peak (cm^{-1})	Assignment	Peak (cm^{-1})	Assignment	Peak (cm^{-1})	Assignment
		727	Wagging vibrations of C-H, C-S, C-C	618	Ring breathing mode II of in-plane deformation of triazine ring	631	Ring breathing mode II of in-plane deformation of triazine ring
855	Wagging vibration of C-H	855	Wagging vibration of C-H	934	Ring breathing mode I of triazine ring	913	Ring breathing mode I of triazine ring
1080	Stretching vibration of C-S	1180	Stretching vibration of C-S	970	Ring breathing	992	Ring breathing
1100	Bending vibration of C-H	1100	Bending vibration of C-H	1516	C-N stretching; Ring C-N stretching; Symmetry NH_2 bending; Asymmetry NH_2 bending	1206-1242	H-N-H rocking
1332	Stretching vibration of N-O	1332	Stretching vibration of N-O			1496	Side chain C-N breathing
1575	Stretching vibration of phenyl ring	1575	Stretching vibration of phenyl ring				

1 M. Li, J. W. Kang, R. R. Dasari and I. Barman, *Angew. Chem. Int. Ed.*, 2014, **53**, 14115 –14119.
2 M. Li, J. W. Kang, S. Sukumar, R. R. Dasari and I. Barman, *Chem. Sci.*, 2015, **6**, 3906–3914.
3 S. Gunasekaran, K. Srinivasan and S. X. J. Raja, *Proc. Indian Natn. Sci. Acsd.*, 1993, **59**, 347-352.
4 E. Koglin, B. J. Kip and R. J. Meier, *J. Phys. Chem.* 1996, **100**, 5078-5089.

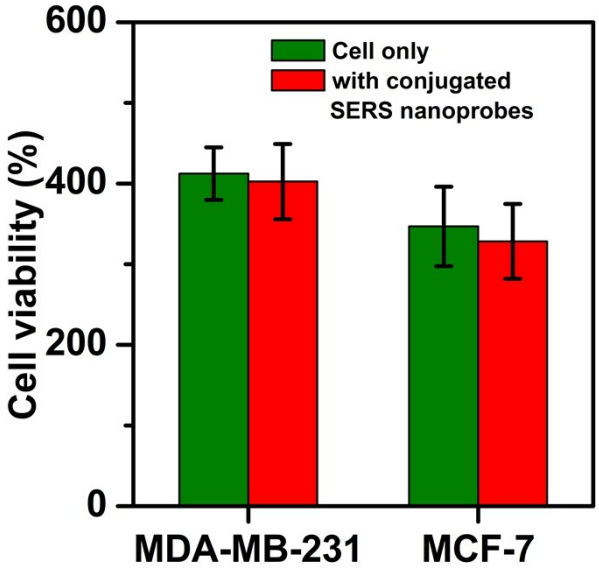

Figure S6. Cell viability of MDA-MB-231 cells and MCF-7 cells incubated with uPAR or EGFR-SERS nanoprobes. MDA-MB-231 cells were incubated with uPAR-SERS nanoprobes (200 pM), and MCF-7 cells were incubated with EGFR-SERS nanoprobes (200 pM). It can be clearly seen that no significant cytotoxicity was observed for both SERS nanoprobes used in this work.

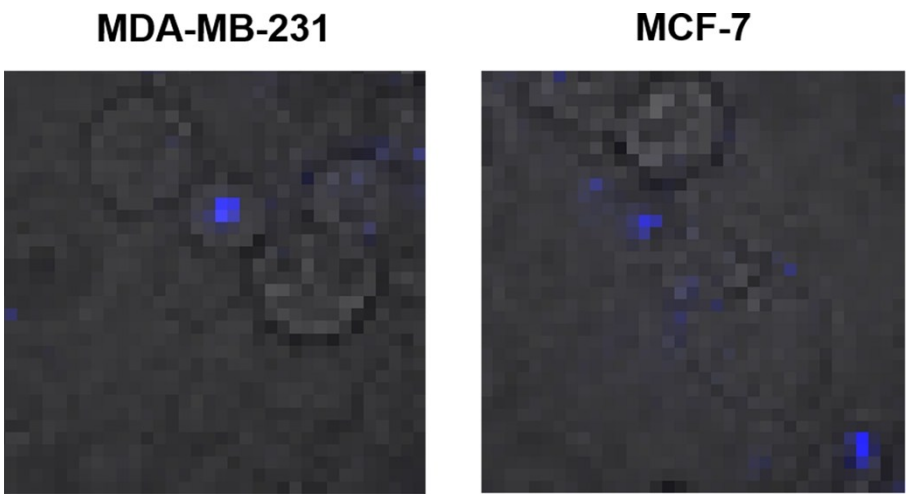

Figure S7. SERS images overlaid with bright-field images of uPAR-SERS nanoprobe-pretreated MDA-MB-231 cells and EGFR-SERS nanoprobe-pretreated MCF-7 cells incubated with unconjugated NTP-encoded SERS nanoprobes (50 pM). It is clearly seen that there is no significant SERS signal observed in both cell lines, indicating high specificity of both SERS nanoprobes toward to uPAR and EGFR expressed on the cell surface.