Supporting Information for:

Self-Assembled Plasmonic Vesicles of SERS-Encoded Amphiphilic Gold Nanoparticles for Cancer Cell Targeting and Traceable Intracellular Drug Delivery

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Calculation of the graft density of polymer brushes on Au nanoparticles. Given the size of a gold atom (0.017nm^3), the number of gold atom ($N_{Au\ atom}$) in 14nm Au nanoparticles can be calculated using Equation S1, where R is the radium of the gold nanoparticles. The result is 84472 gold atoms per nanoparticle and therefore the molar mass ($M_{Au\ nanoparticle}$) of the gold nanoparticle is $197N_{Au\ atom}$. Combining the molar mass of the gold nanoparticle, the ratio of PEG and PMMA and the weight fraction obtained in TGA analysis, the average number of polymer grafts can be calculated by Equation S2, where $W_{polymer}$ is the weight fraction (21%) of the organic part, $W_{Au\ nanoparticle}$ is the weight fraction of gold nanoparticle and $M_{PEG+2PMMA}$ is the sum of the molar mass of one PEG and two PMMA grafts. The result is 246 grafts per nanoparticle, which include 82 PEG chains and 164 PMMA chains, and the graft density is ~0.4 chain/nm^2.

$$N_{Au\ atom} = \frac{V_{Au\ nanoparticle}}{V_{Au\ atom}} = \frac{4\pi}{3}\left(\frac{R^3}{V_{Au\ atom}}\right) \qquad \textit{(Equation S1)}$$

$$N_{\text{grafts per nanoparticle}} = \left(\frac{{}^{3W_{polymer}}/_{M_{PEG+2PMMA}}}{{}^{W_{Au\ nanoparticle}}/_{M_{Au\ nanoparticle}}}\right) \qquad (\textit{Equation S2})$$

Calculation of the ensemble-averaged enhancement factor (EF) of the SERS-active plasmonic vesicles. EF was calculated using the equation, $EF = (I_{SERS} \times N_{normal})/(I_{normal} \times N_{SERS})$, where I_{SERS} and I_{normal} are the peak intensity at 1615 cm^{-1} of BGLA spectra obtained from the vesicles and the aqueous solution respectively, and N_{SERS} and N_{normal} are the corresponding number of BGLA molecules in the scattering volume. N_{normal} was calculated by the following equation, $N_{normal} = C_{normal} \times V_{scattering}$, where C_{normal} is the concentration of BGLA solution, and $V_{scattering}$ is the scattering volume of the focused laser beam. N_{SERS} was estimated by the following equation, $N_{SERS} = N \times C_{Au\ NPs} \times V_{scattering}$, where N is the average number of BGLA on each 14 gold nanoparticles, $C_{Au\ NPs}$ is the concentration of 14 nm gold nanoparticles in the vesicles dispersion, and $V_{scattering}$ is the scattering volume of the focused laser beam. As a result, EF can be calculated by the following equation, $EF = (I_{SERS} \times C_{normal})/(I_{normal} \times N \times C_{Au\ NPs})$.

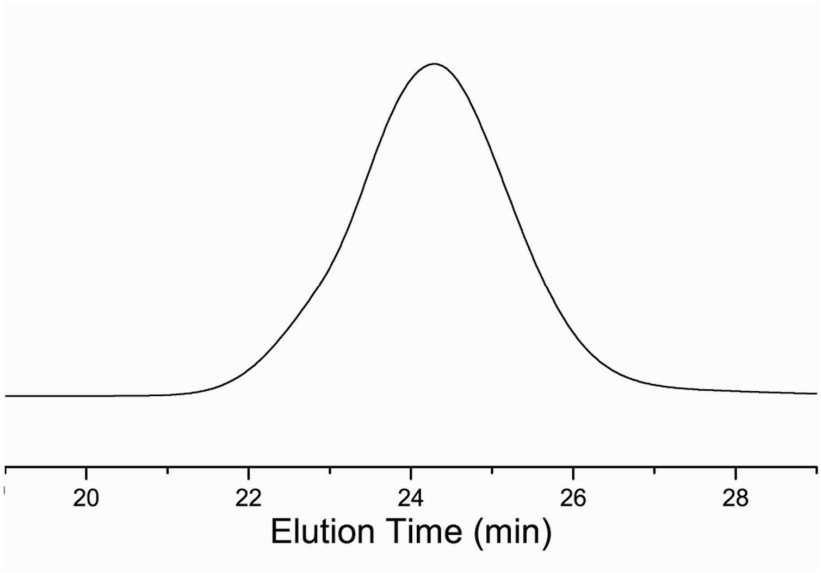

Figure S1. GPC trace of the copolymer of methyl methacrylate (MMA) and 4-vinyl pyridine (4VP) detached from the gold nanoparticles (M_n=24 kDa, PDI=1.21).

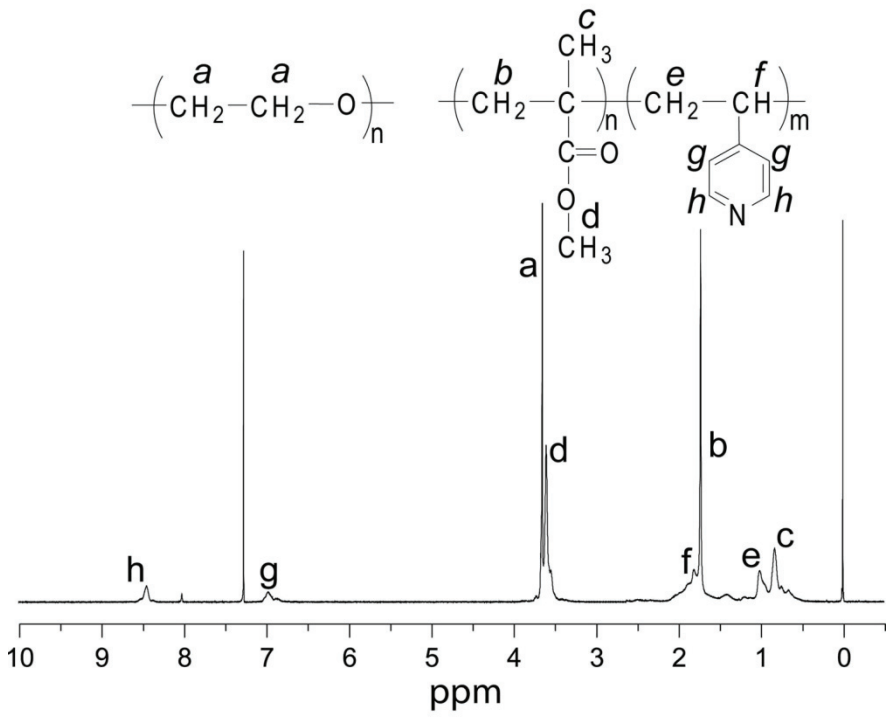

Figure S2. ^{1}H NMR (300 MHz, δ, ppm, $CDCl_3$) of the amphiphilic gold nanoparticles coated with mixed polymer brushes of poly(ethylene glycol) and copolymer of methyl methacrylate (MMA) and 4-vinyl pyridine (4VP): 8.46 and 6.91 (*pyridine*), 3.67 (-OCH_2CH_2-), 3.62 (-OCH_3), 2.25 (-C*H*), 1.24-2.16 (-CH_2), 1.26 (-CH_2), 0.36-1.27 (-CH_3). The ratio of MMA and 4VP in the copolymer was calculated based on the resonance of pyridine (8.45 ppm) and that of -CH_3 group (0.36-1.27 ppm) of MMA, leading to 10% of 4VP in the copolymer.

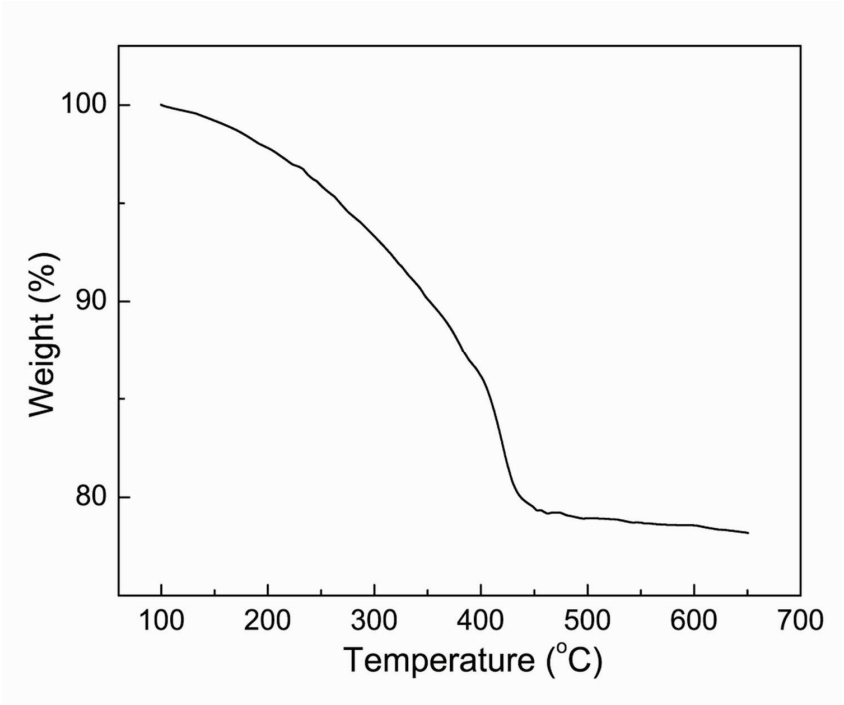

Figure S3. TGA analysis of the gold nanoparticles grafted with mixed polymer brushes of poly(ethylene glycol) and copolymer of methyl methacrylate (MMA) and 4-vinyl pyridine (4VP) (the weight fraction of the polymer brushes is 21%).

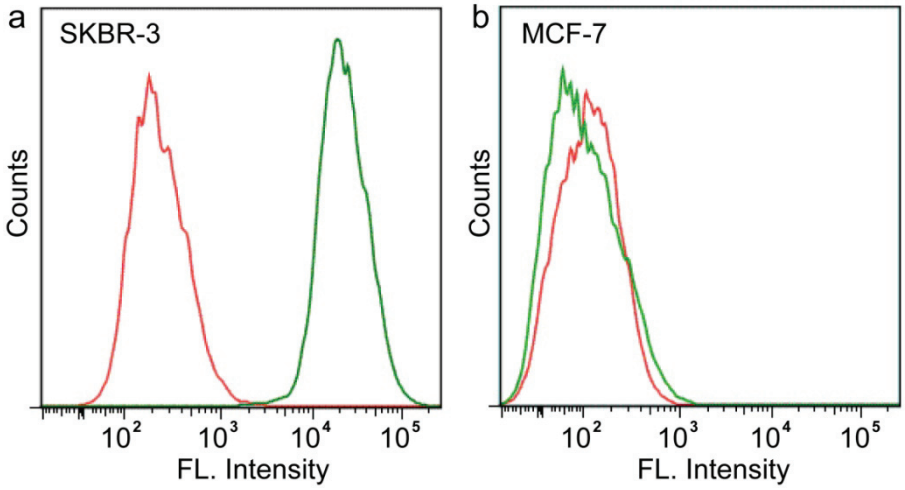

Figure S4. The flow cytometric analyses of SKBR-3 (a) and MCF-7 (b) cells labelled with a HER2 antibody and an Alexa Fluor® 594-conjugated secondary anti-mouse antibody (green line) and control cells (red line) incubated with normal mouse IgG1.

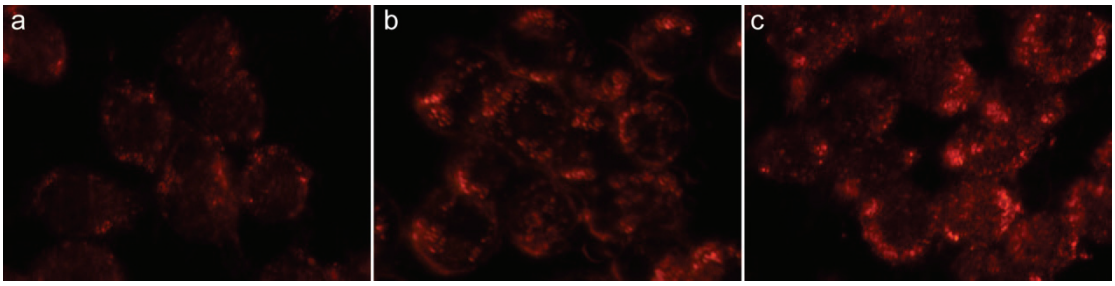

Figure S5. Dark-field images of SKBR-3 cells incubated with targeted vesicles for 10, 30, and 90 min.

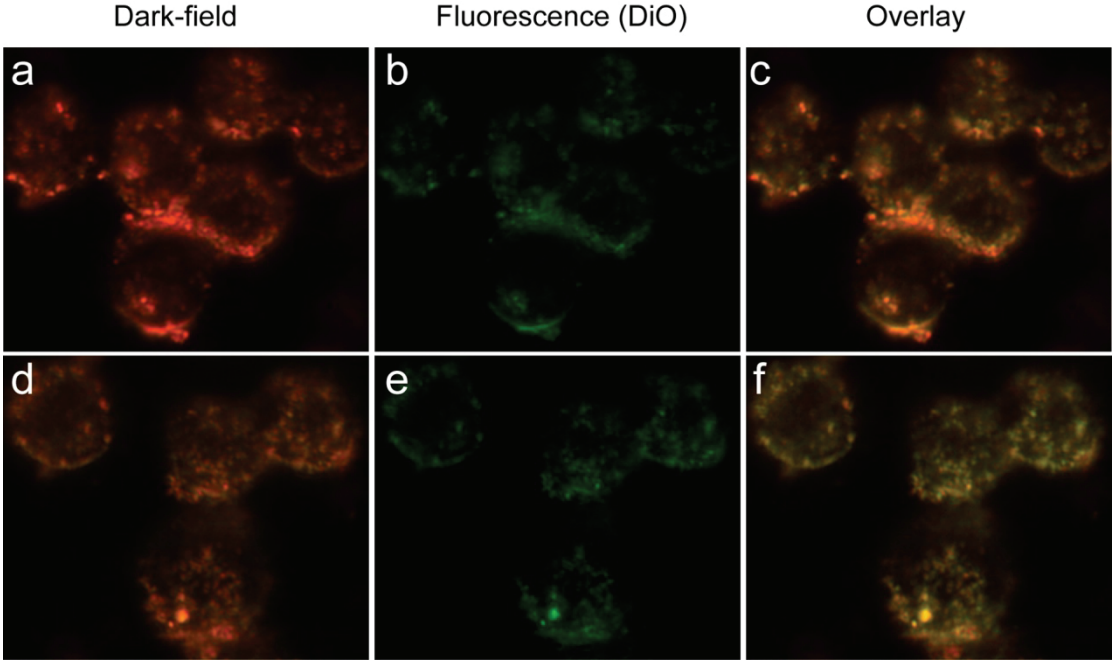

Figure S6. The co-localization of the plasmonic vesicles and the organelle-tracking dye DiO in SKBR-3 cells incubated with targeted vesicles for 30 min (a-c) and 60 min post-incubation (d-f).

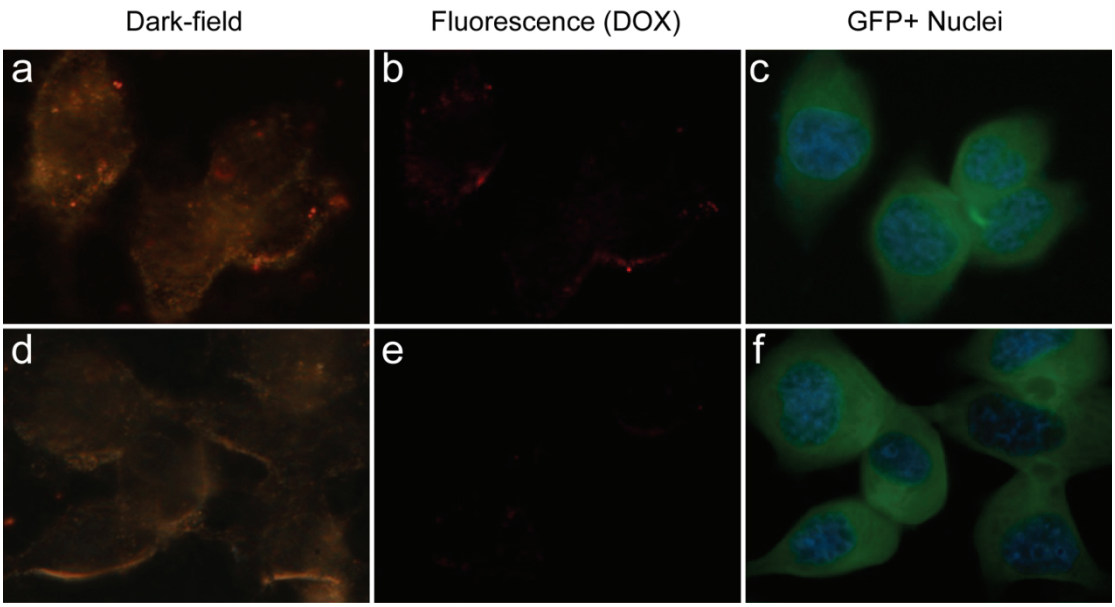

Figure S7. Dark-field (a, d), fluorescence (b, e), and the overlaid GFP and DAPI images (c, f) of MCF-7 cells labeled with DOX-loaded pH-sensitive plasmonic vesicle after incubated with targeted vesicles for 30 min (a-c) and 60 min post-incubation (d-f).