Supporting Information

Investigating the Intracellular Behaviors of Liposomal Nanohybrids *via* SERS: Insights into the Influence of Metal Nanoparticles

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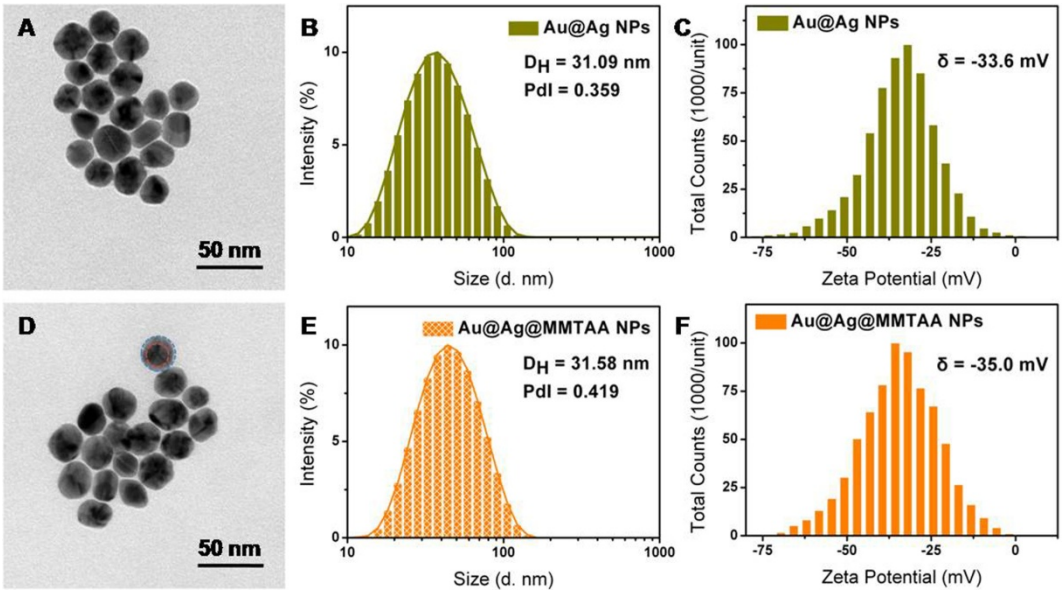

Figure S1. Characterization of Au@Ag nanoparticles (A-C) and Au@Ag@MMTAA nanoparticles (D-F): (A, D) TEM, (B, E) size distribution and (C, F) surface zeta potential.

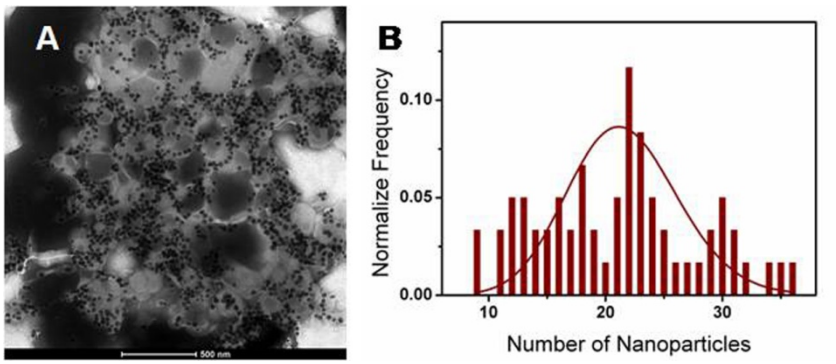

Figure S2. (A) Large-scale TEM image of liposome-metal nanohybrids. (B) Distribution for the number of metal

nanoparticle per nanohybrid and the corresponding fit curve.

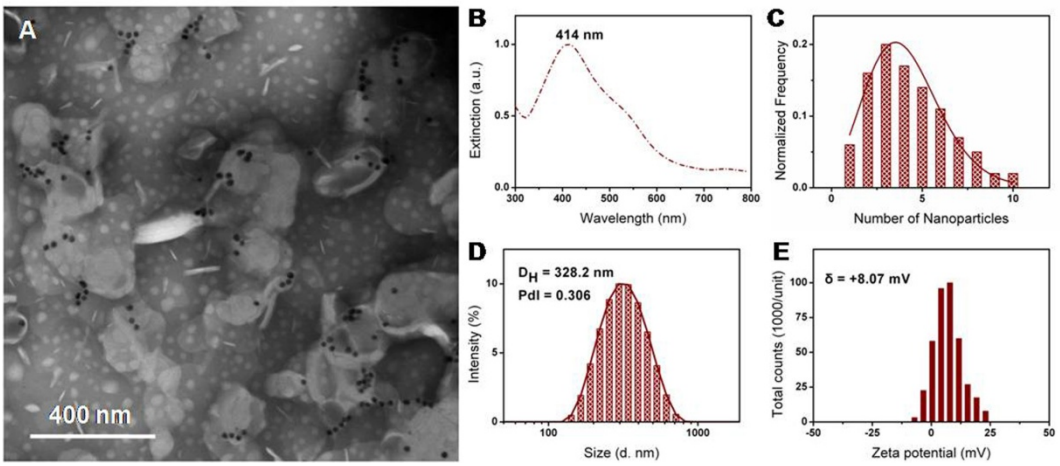

Figure S3. Characterization of liposome-metal nanohybrids with low coverage: (A) large-scale TEM image, (B) extinction spectrum, (C) distribution for the number of metal nanoparticle per nanohybrid, (D) size distribution and (E) surface zeta potential.

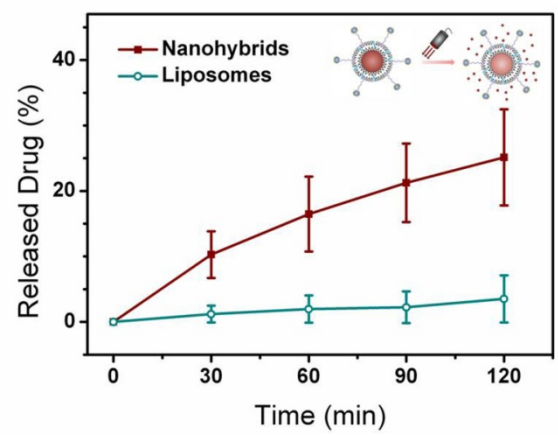

Figure S4. Drug release profiles of liposomes and nanohybrids under laser irradiation.

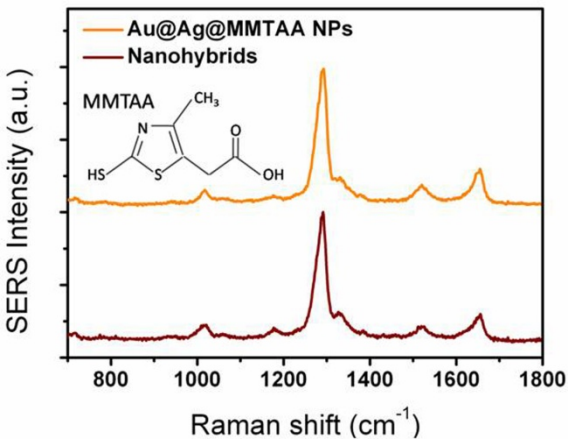

Figure S5. SERS spectra of Au@Ag@MMTAA nanoparticles and nanohybrids.

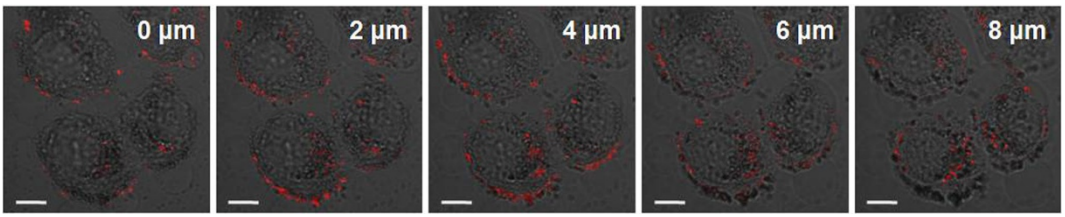

Figure S6. The merged images of SERS and bright field at different depths of SKBR3 cells using a confocal laser scanning microscope. Scale bars for confocal images are 10 μm.

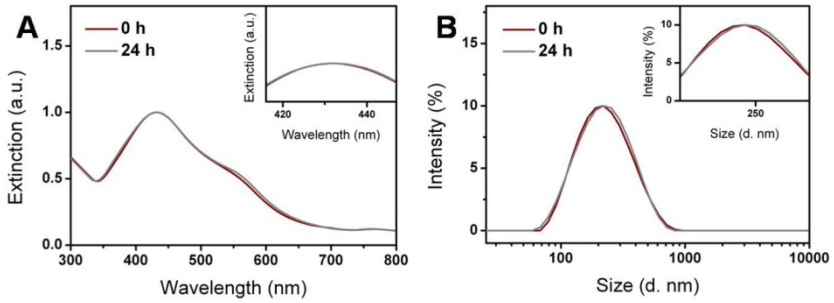

Figure S7. Colloidal stability of nanohybrids during incubation at 37 °C for 24 h in PBS: (A) extinction property and (B) size distribution.

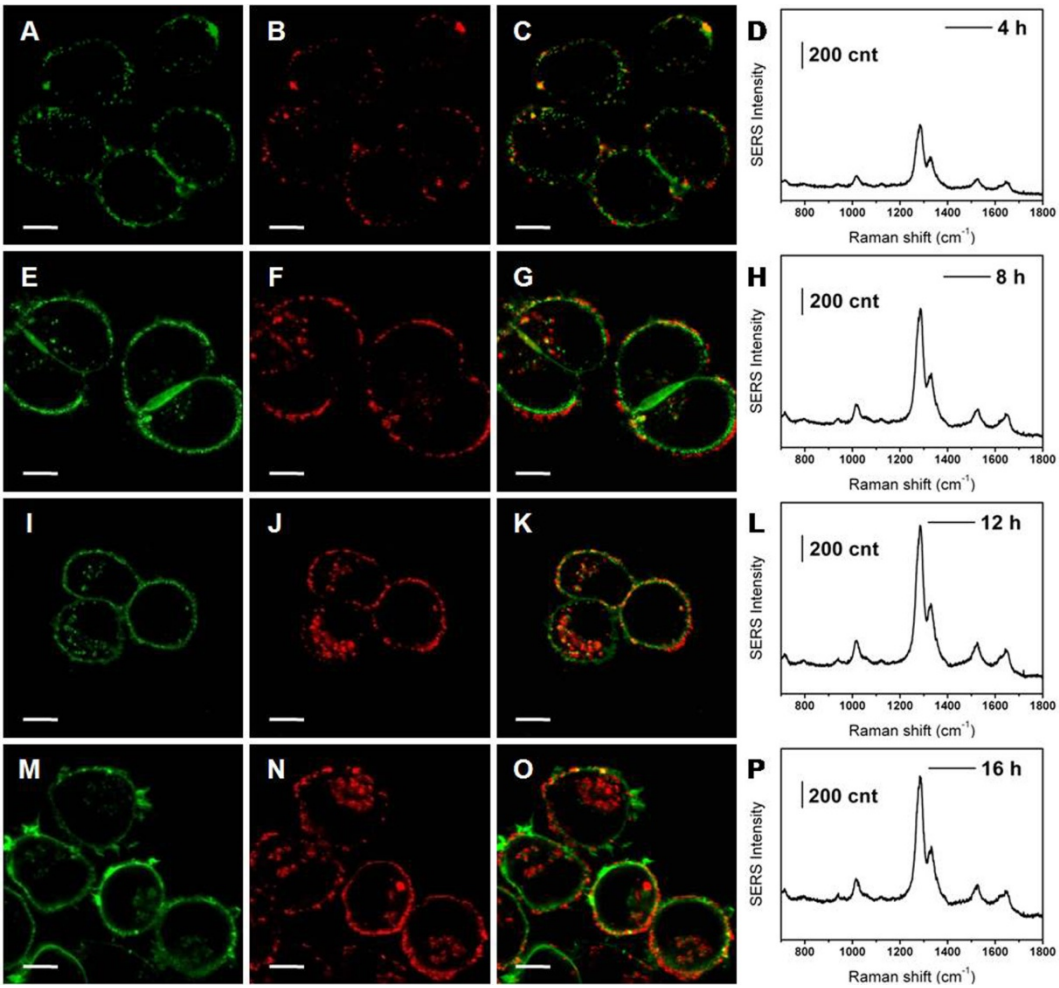

Figure S8. Confocal microscopy of SERS labeled nanohybrids (red) and DiI labeled cell membranes (green) for 4 h (A-C), 8 h (E-G), 12 h (I-K) and 16 h (M-O). In the intracellular experiments, 580-610 nm light was collected for fluorescence imaging of DiI (green) and 800-1600 cm^{-1} Raman scattered light was collected for SERS imaging (red). D, H, L and P are the average spectrum corresponding to the different time point. Scale bars for confocal images are 10 μm.

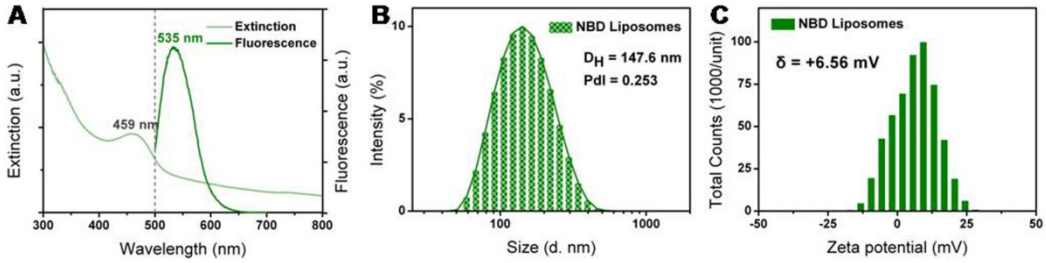

Figure S9. Characterization of fluorescence-labeled NBD liposomes: (A) extinction and fluorescence spectra, (B) size distribution and (C) surface zeta potential.

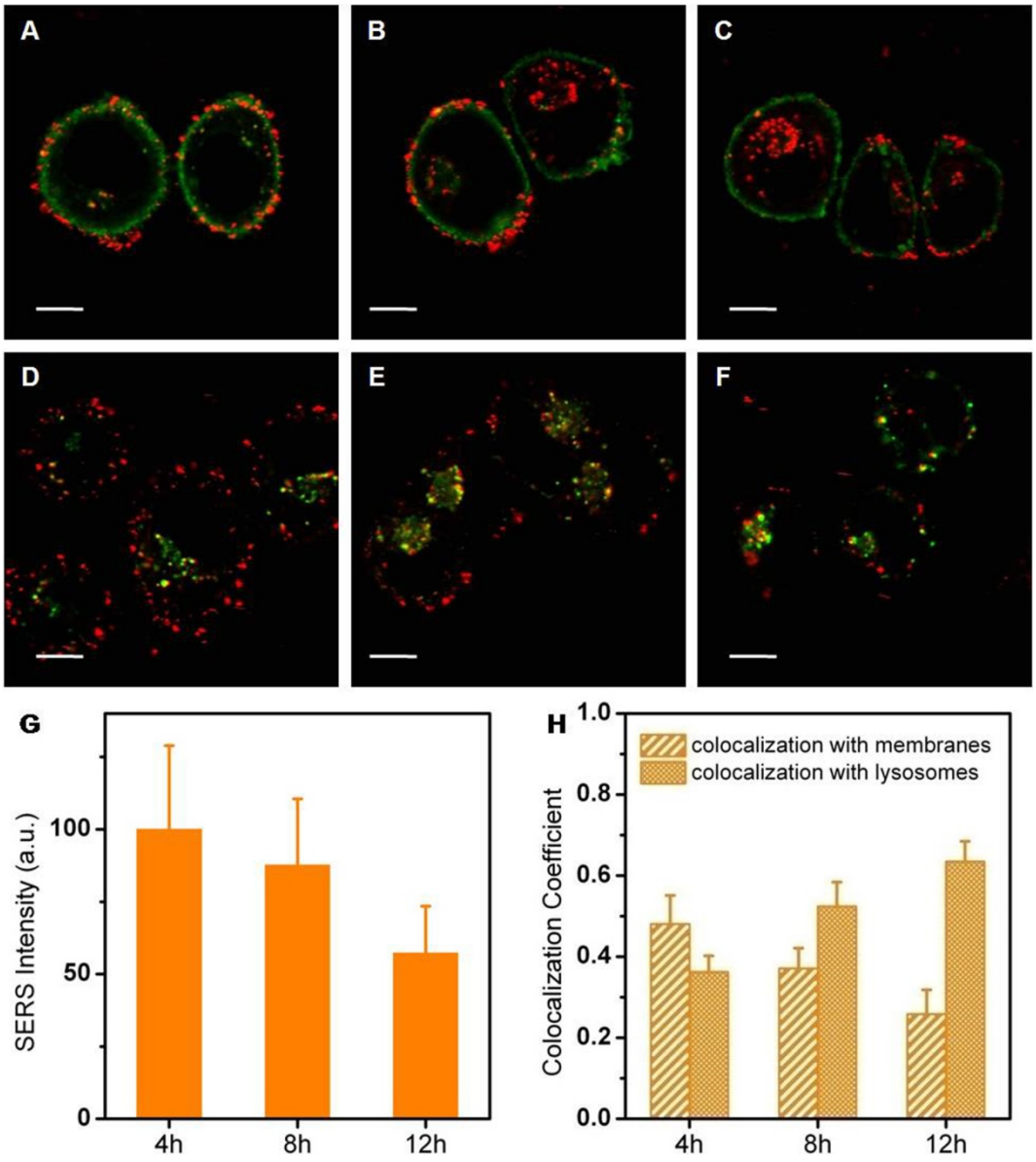

Figure S10. Confocal microscopy of SERS labeled metal nanoparticles (red) and fluorescence staining of organelle markers (green). Makers are DiL (membranes, A-C) and Lyso-tracker green (lysosomes, D-F); 500-540 nm light was collected for the fluorescence imaging of Lyso-tracker Green, 580-610 nm light was collected for fluorescence imaging of DiI and 800-1600 cm^{-1} Raman scattered light was collected for SERS imaging. (G) Average SERS intensity of a single SKBR3 cell incubated with the nanohybrids for 4, 8 and 12 h. (H) Colocalization coefficients between nanoparticles and membranes (or lysosomes). Scale bars for confocal images are 10 μm.

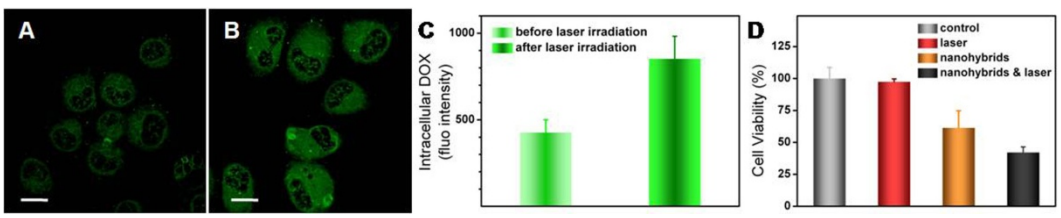

Figure S11. Fluorescence images of DOX (green) in nanohybrids treated SKBR3 cells without (A) and with (B) laser irradiation: 500-600 nm light was collected for fluorescence imaging of DOX. Scale bars for confocal images are 20 μm. (C) Average fluorescence intensity of DOX per cell before and after laser irradiation. without or with laser irradiation. (D) Photothermal cytotoxicity (quantitative analysis - MTT assay). SKBR3 cells incubated with standard culture media were used as a control.