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# Supporting Information

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# Reversibly Extracellular pH Controlled Cellular Uptake and Photothermal Therapy by PEGylated Mixed-Charge Gold Nanostars

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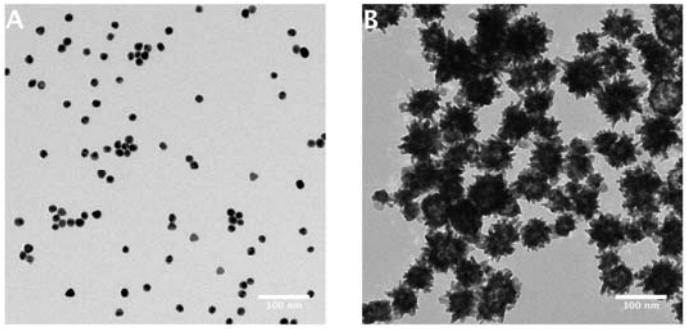


**Figure S1.** TEM images of gold particles (A) and gold nanostars (B) prepared by growth of gold particles. Scale bar: 100 nm.

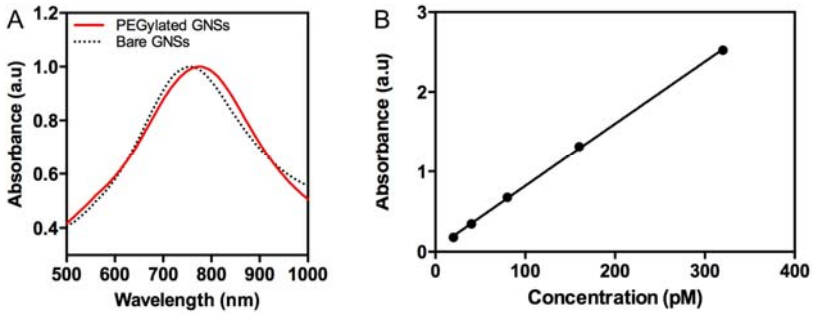


**Figure S2.** (A) UV-Vis spectra of GNSs before and after PEGylation. (B) Plot of absorbance of PEGylated GNSs at 780 nm vs. their concentration.

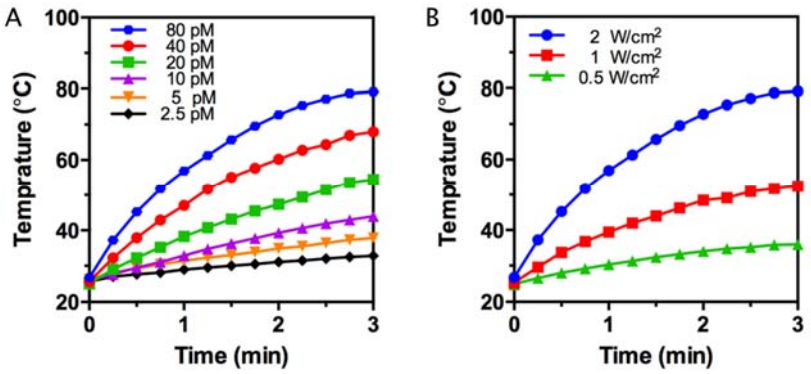


**Figure S3.** (A) Heating curves of GNS-N/C **4** solution at concentration of 2.5, 5, 10, 20, 40 and 80 pM upon 808 nm laser irradiation at 2 W/cm$^2$ for 3 min. (B) Heating curves of GNS-N/C **4** solution (80 pM) upon 808 nm laser irradiation at 0.5, 1 and 2 W/cm$^2$ for 3 min.

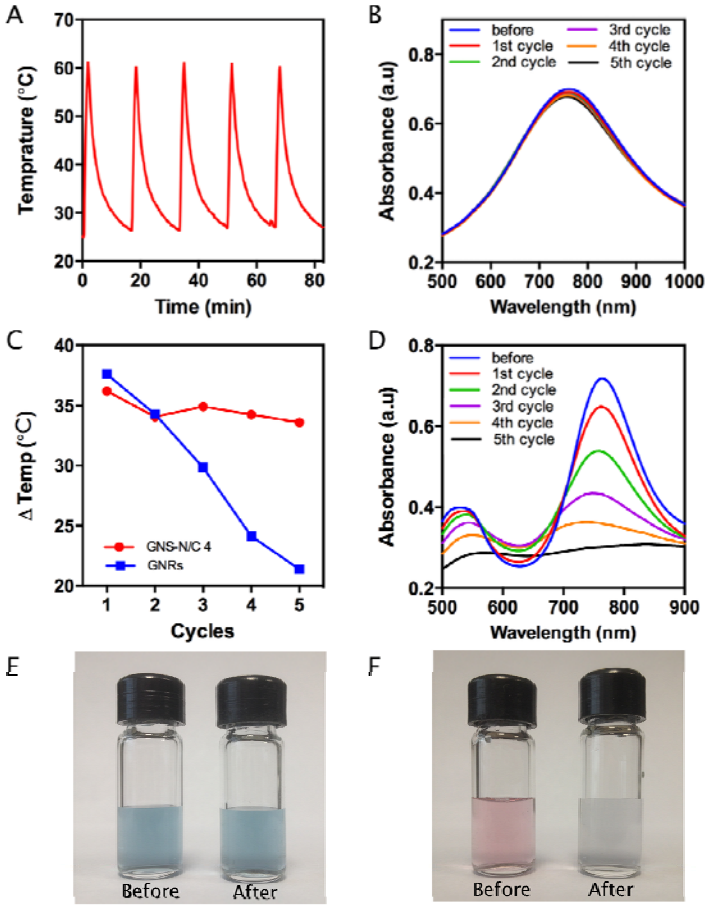

**Figure S4.** (A) Heating curves of GNS-N/C **4** solution (80 pM) irradiated by an 808 nm laser (2 W/cm$^2$) for five ON-OFF cycles (ON: 1.5 min, OFF: 15.5 min). (B) Corresponding UV-Vis spectra of GNS-N/C **4** solution before irradiation and at the end of each cycle of irradiation. (C) Change of temperature of GNS-N/C **4** (40 pM, ~0.7 OD) and PEGylated GNRs (~0.7 OD) at the end of each laser heating cycle for five cycles. (D) Corresponding UV-Vis spectra of PEGylated GNRs solution before and at the end of each laser heating cycle. Digital photos of GNS-N/C **4** (E) and PEGylated GNRs (F) after five cycles of laser heating.

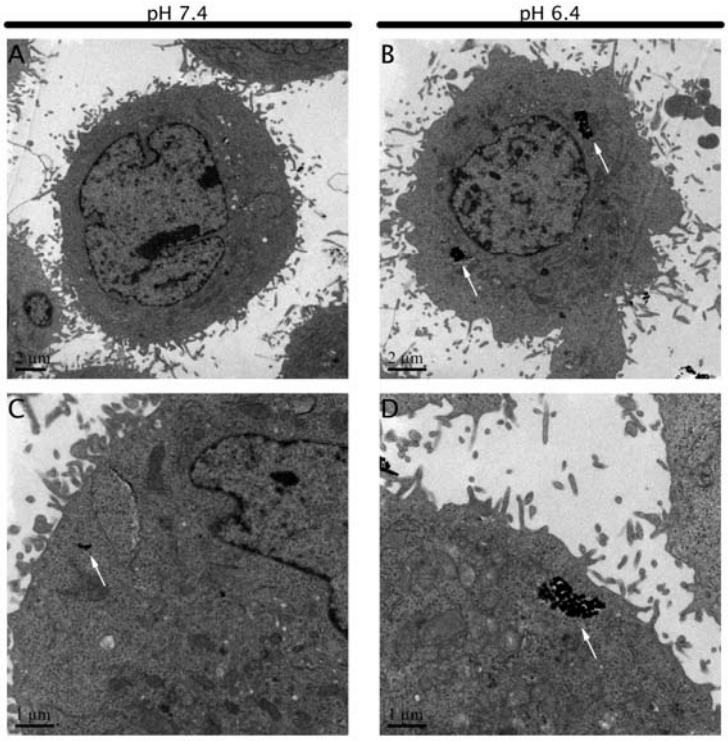


**Figure S5.** TEM images of HeLa cells incubated with 80 pM GNS-N/C **4** at pH 7.4 (A, C) or pH 6.4 (B, D). White arrows indicate GNSs in cells.

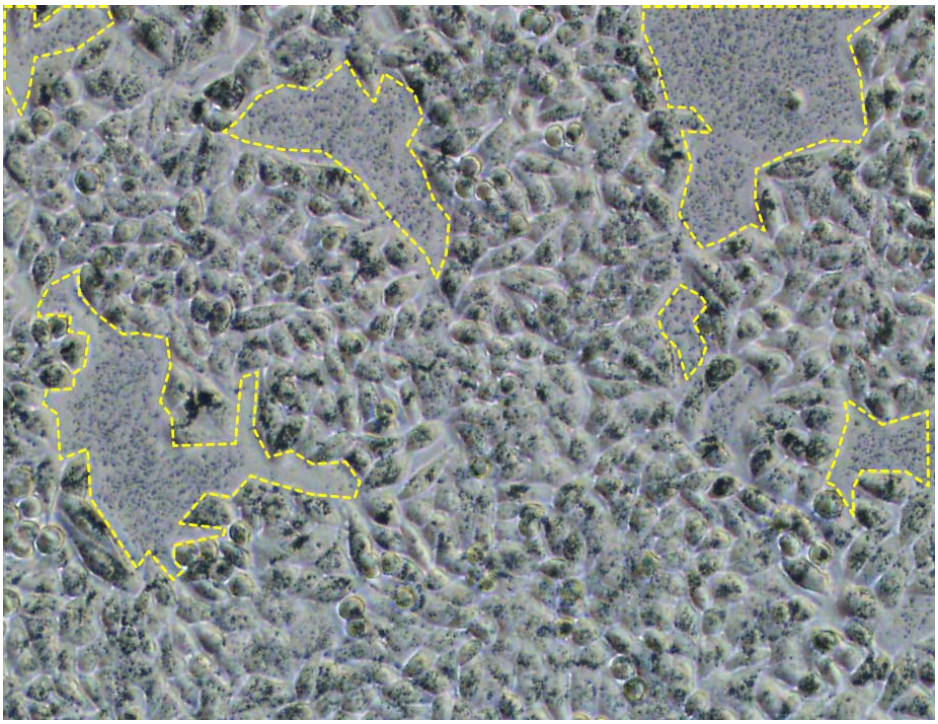

**Figure S6.** Optical microscopic image of HeLa cells after incubation with GNS-$NH_2$ for 4 h. The background circled in dashed lines showed plenty of aggregations attached to the substrate of cell culture dish.

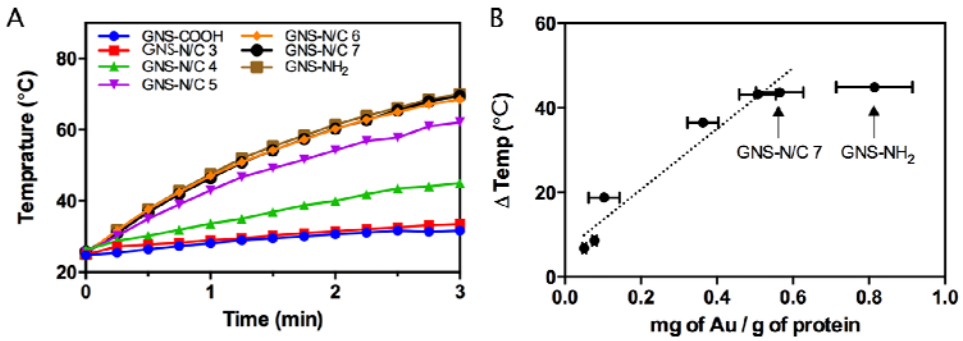


**Figure S7.** (A) Heating curves of cell suspensions in PBS upon 808 nm laser irradiation at 2 W/$cm^2$ for 3 min. Cells were incubated with GNS-$NH_2$, GNS-COOH, GNS-N/C **3-7** at concentration of 80 pM for 4 h, then washed and resuspended in equal volume of PBS. (B) Plot of the change of temperature as a function of the degree of cellular uptake. The

linear relationship between the change of temperature and the uptake of PEGylated mixed-charge GNSs is depicted in dash line. $R^2 = 0.94$.

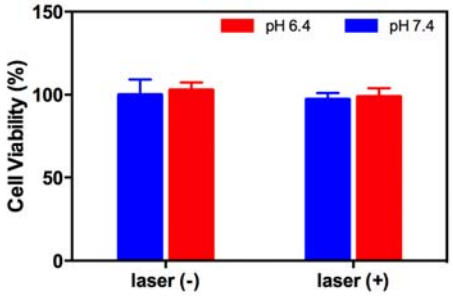


**Figure S8.** Cell viability of HeLa cells incubated in DMEM at pH 6.4 or 7.4 for 4 h with or without laser irradiation at 2 W/cm$^2$ for 3 min.

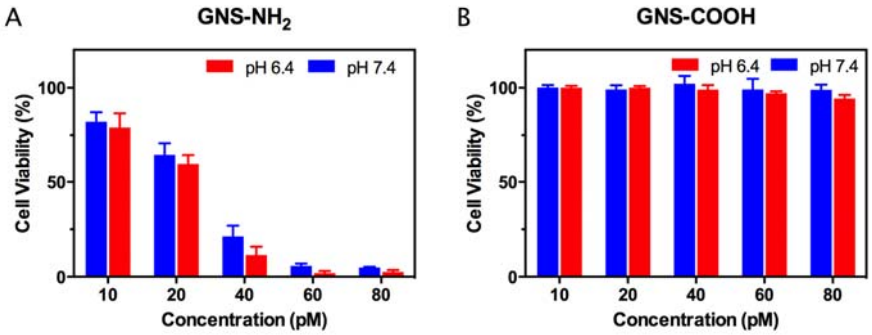


**Figure S9.** Cell viability of HeLa cells incubated with 80 pM GNS-$NH_2$ or GNS-COOH at pH 6.4 or 7.4 for 4 h followed by 808 nm laser irradiation at 2 W/cm$^2$ for 3 min.

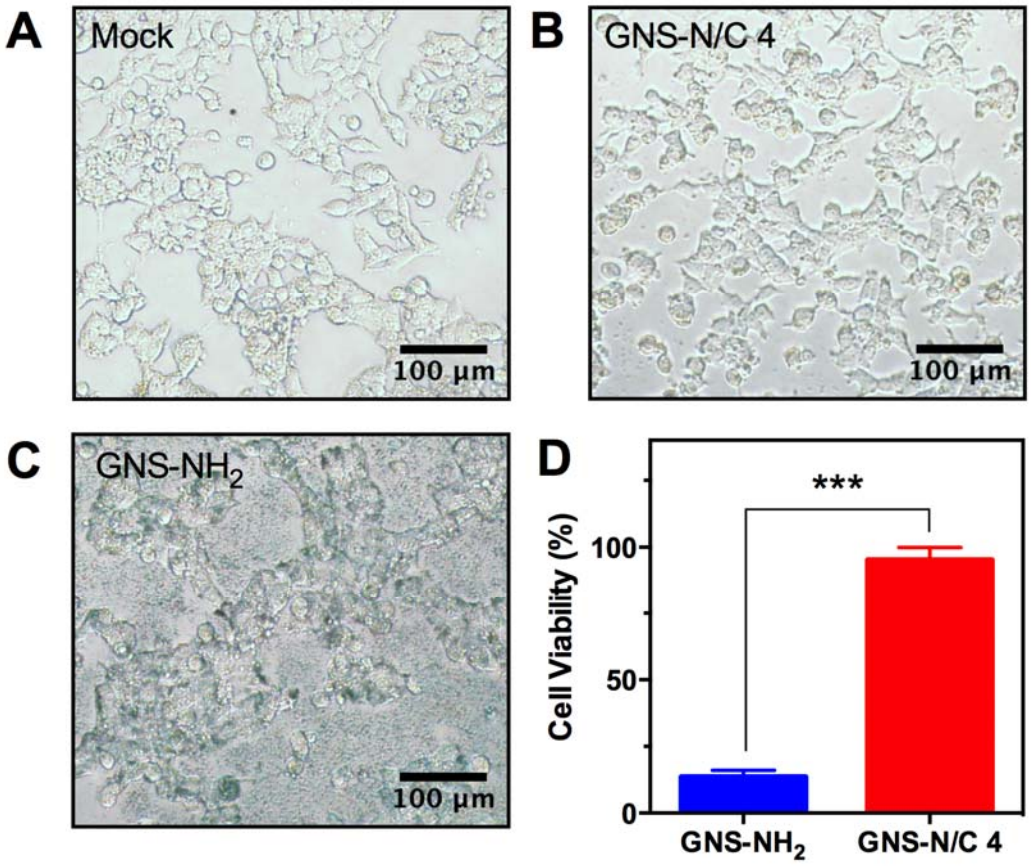


**Figure S10**. Optical microscopic images of 293T cells incubated with nothing (A) or 80 pM of GNS-N/C **4** (B) or GNS-$NH_2$ (C) for 4 h. The background of (C) is dark due to the aggregation of GNS-$NH_2$ attached on the substrate of cell cultural dish. (D) Cell viability of 293T cells incubated with GNS-N/C **4** or GNS-$NH_2$ after laser irradiation (808 nm, 2 W/$cm^2$, 3 min). Asterisks (***) denote statistically significant difference ($p < 0.001$) calculated with two-sample t-test.

## Supplementary Tables

**Table S1.** Hydrodynamic diameters of bare GNSs and PEGylated GNSs in water.

| | **DLS sizes (nm)** | | **DLS sizes (nm)** |
|---|---|---|---|
| **Bare GNSs** | 77.5 ± 3.2 | **PEGylated GNSs**[a)] | 94.3 ± 4.3 |
| **GNS-$NH_2$** | 92.2 ± 3.4 | **GNS-N/C 3** | 95.4 ± 3.1 |
| **GNS-N/C 4** | 91.6 ± 5.8 | **GNS-N/C 5** | 94.7 ± 3.7 |
| **GNS-N/C 6** | 95.7 ± 5.0 | **GNS-N/C 7** | 95.8 ± 6.6 |
| **GNS-COOH** | 94.3 ± 4.7 | | |

[a)]Hydrodynamic diameter of PEGylated GNSs is calculated as the average of hydrodynamic diameters of GNS-$NH_2$, GNS-COOH, GNS-N/C **3-7**.

**Table S2.** Hydrodynamic diameters of GNS-N/C **4**, GNS-COOH, GNS-N/M and GNS-$NH_2$ after incubation in pH 7.4 DMEM for three days.

| | **DLS sizes (nm)** | | **DLS sizes (nm)** |
|---|---|---|---|
| **GNS-N/C 4** | 104.0 ± 3.7 | **GNS-COOH** | 106.7 ± 6.2 |
| **GNS-N/M** | 125.3 ± 8.9 | **GNS-$NH_2$** | 343.2 ± 14.8 |