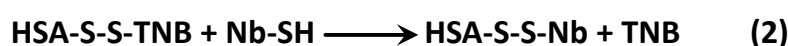


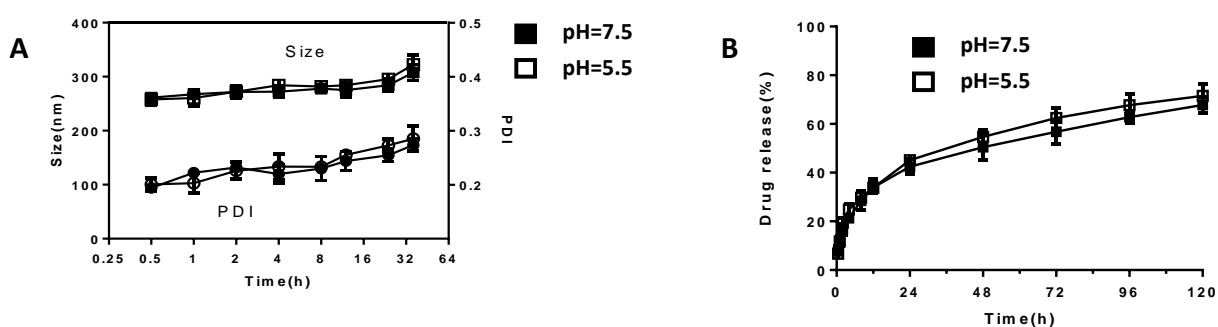
## Supporting Information

for

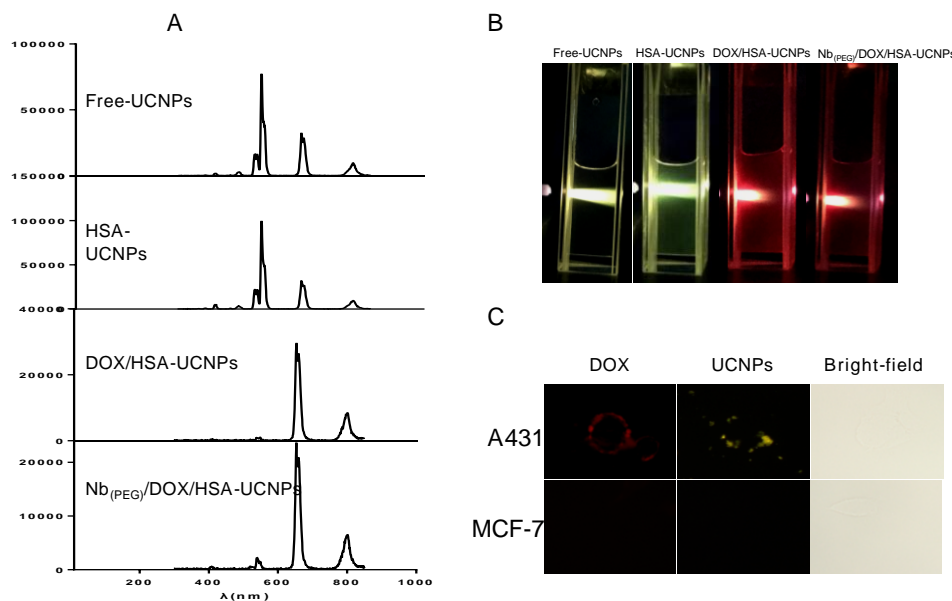
### Transglutaminase mediated PEGylation of nanobody for targeted nano-drug delivery



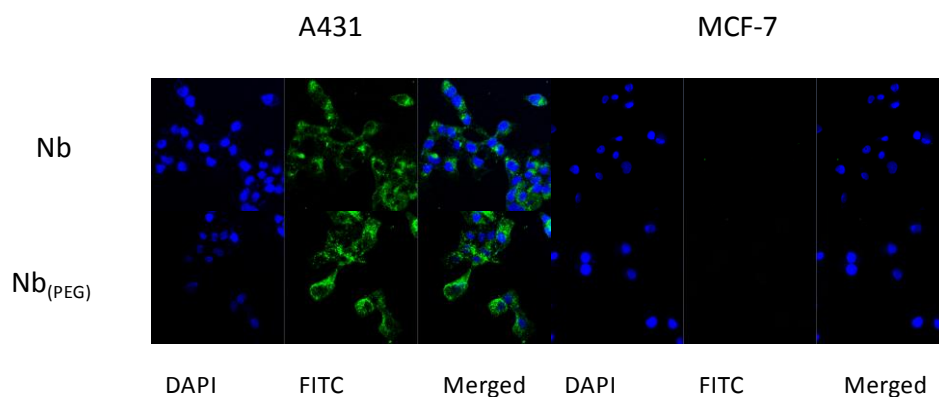
**Figure S1.** Illustration of the formation of HSA-Nb conjugates via hetero-disulfide bonds by DTNB and the reduction by reducing agents.



**Figure S2.** A) The time dependent measurement of particle size and PDI of Nb(PEG)/DOX/HSA-UCNPs. Particles were incubated in DMEM medium containing 10% FBS at 37 °C. Error bars denote standard deviations of three independent experiments. B) In vitro drug release of DOX from Nb(PEG)/DOX/HSA-UCNPs in PBS at 37 °C. Error bars denote standard deviations of three independent experiments.



**Figure S3.** The upconversion emission spectrum of Nb<sub>(PEG)</sub>/DOX/HSA-UCNPs. (A) The upconversion fluorescence spectra of free UCNPs, HSA-UCNPs, DOX/HSA-UCNPs and Nb<sub>(PEG)</sub>/DOX/HSA-UCNPs at the same concentration (2 mg/mL) under excitation with a 980 nm laser. (B) Photos of free UCNPs, HSA-UCNPs, DOX/HSA-UCNPs and Nb<sub>(PEG)</sub>/DOX/HSA-UCNPs under excitation with a 980 nm laser. (C) Fluorescence images of A431 cells and MCF-7 cells incubated with Nb<sub>(PEG)</sub>/DOX/HSA-UCNPs (1.5 mg/mL) at 4 °C for 3 h under excitation of 561 nm for DOX and 980 nm for upconversion.



**Figure S4.** Cellular binding and internalizing measurements. CLSM images of Nb and Nb<sub>(PEG)</sub> on A431 cells and MCF-7 cells.