Materials:

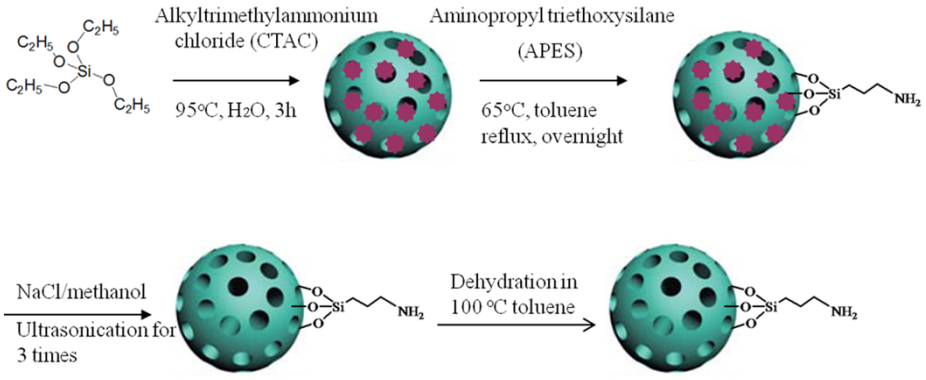
Diisopropylcarbodiimide (DIC), diisopropylethylamine (DIPEA), cetyl trimethylammonium chloride (CTAC), triethanolamine (TEA), poly(ethylene glycol) methyl ether methacrylate (Mw：~475) (PEGMA), 2-(dimethylamino)ethyl acrylate (DMAEA) and aminopropyltriethoxysilane (APES) were purchased from Sigma-Aldrich. Doxorubicin (DOX) was provided by Beijing HuaFeng United Technology Co., Ltd. PBS solution (10 mmol/L, pH 7.2-7.4) was purchased from Beijing Zoman Biotechnology Co., Ltd. The water was deionized.

***In vivo* Experiment Process:**

In the *in vivo* distribution experiment for VX_2 tumor-bearing New Zealand rabbits, 6 rabbits were randomly divided to 2 group (n=3). The sample at the dose of 15 mg was injected intravenously into the ear margin. At 24 h after injection, the Si concentration measurement was carried out as above in the nude mice experiment. To obtain the blood half-life of the MSN-PEG and MSN-PEG+, the blood of each rabbit were collected using the disposable hemostix in 2 min, 5 min, 10 min, 30 min, 1h, 2h and 24 h. 0.5 ml of blood sample were collected every time and the Si concentration were measured using ICP.

Physical characterization:

TEM images were obtained by using JEM-2100F electron microscope operating at 200 kV. UV-vis absorption spectrum was measured on a UV-3101PC Shimadzu UV-vis spectroscope. Fluorescence images were collected on a FV1000 Olympus fluorescence confocal microscope. Particle size and z-potential were obtained by Zetasizer (Malvern, Nano-ZS90). The thermo-gravimetric analysis (TG) data were obtained by NETZSCH STA 449C. N_2 adsorption-desorption isotherms at 77 K were measured on a Micrometitics Tristar 3000 system. Specific surface area was calculated by using Barrett-Joyner-Halenda (BJH) and Langmuir methods, respectively.



Scheme S1: Synthetic procedure of MSN-NH_2.

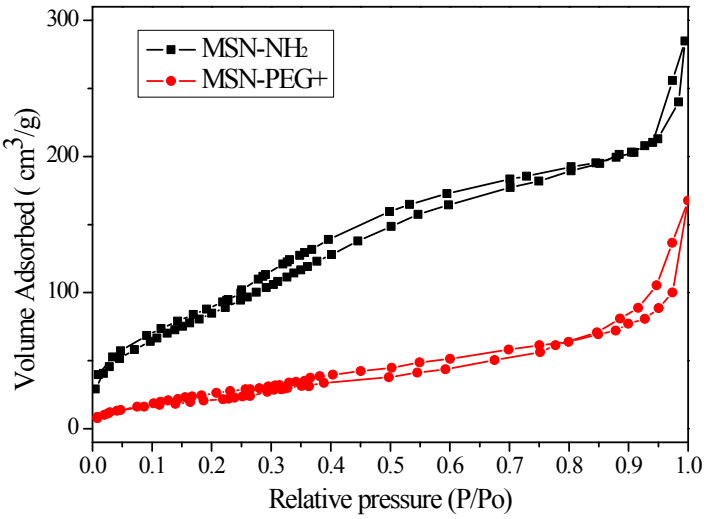


Figure S1. N_2 adsorption–desorption isotherms of MSN-NH_2 and MSN-PEG+. The BET surface area is 571.6 m^2/g and 179.2 m^2/g.

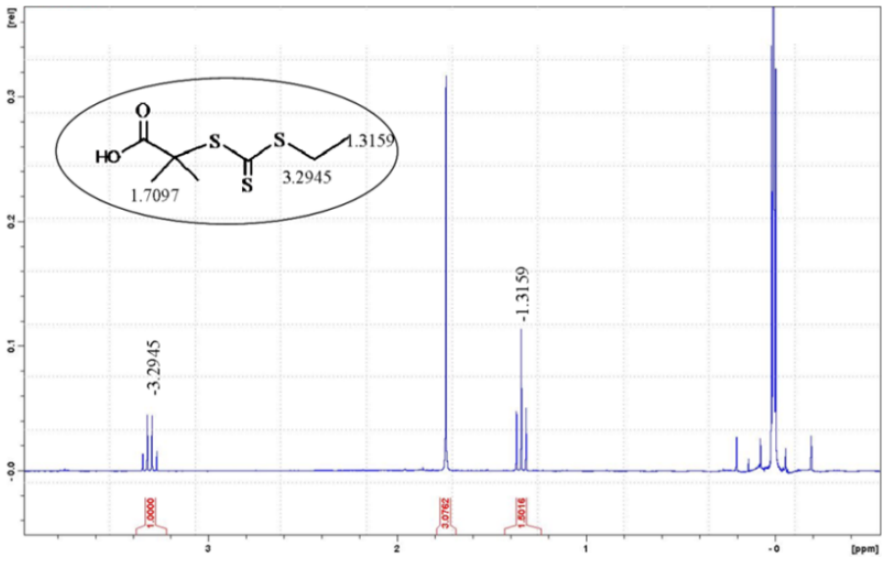


Figure S2. Chemical structure and ^{1}H-NMR spectra of S-Ethyl-S'(α,α'-dimethyl-α"-acetic acid)trithiocarbonate. Successful synthesis of this RAFT agent was confirmed by ^{1}H-NMR (300 MHz, $CDCl_3$) 3.29 ppm (q, 2H), 1.71 ppm (s, 6H) and 1.32 ppm (t, 3H).

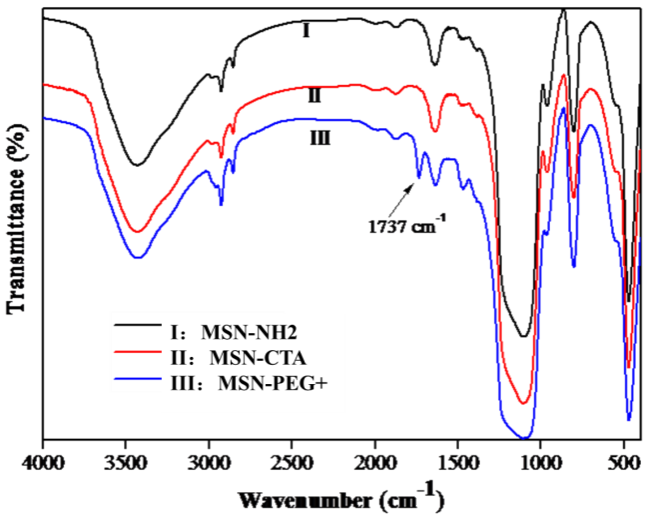


Figure S3. Fourier Transform Infrared (FTIR) spectrum of (I) MSN-NH_2, (II) MSN-CTA and (III) MSN-PEG+. The peak at 1737 cm^{-1} is consistent with the C=O vibration of copolymer.

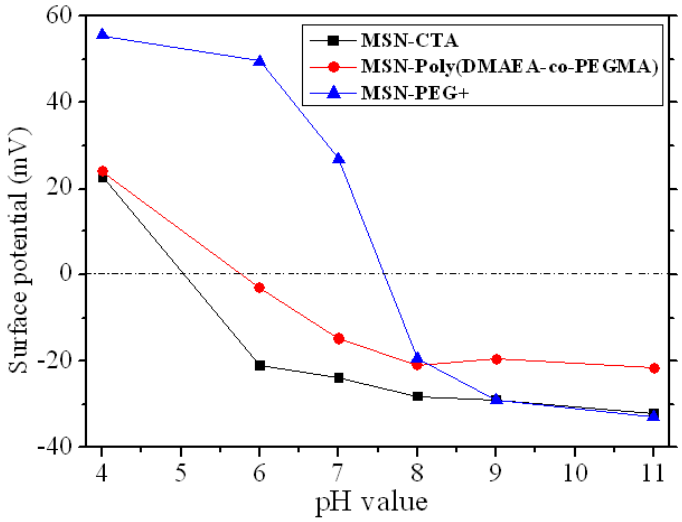


Figure S4. The zeta potential as a function of pH value in aqueous solution of MSN-CTA, MSN-Poly(DMAEA-co-PEGMA) and MSN-PEG+.

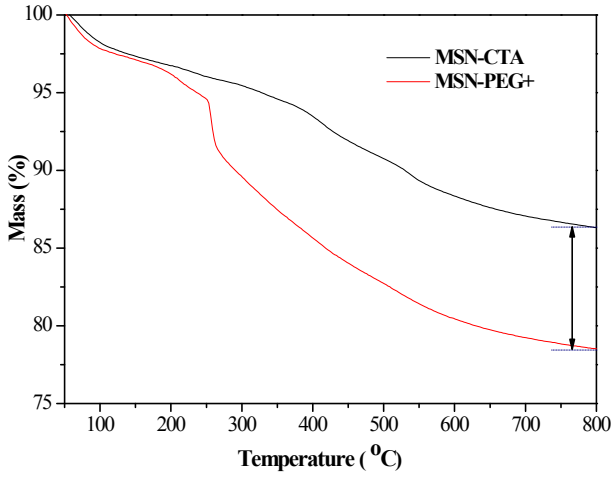


Figure S5. TG curves of MSN-CTA and MSN-PEG+ showing ~8.0 % copolymer content in MSN-PEG+.

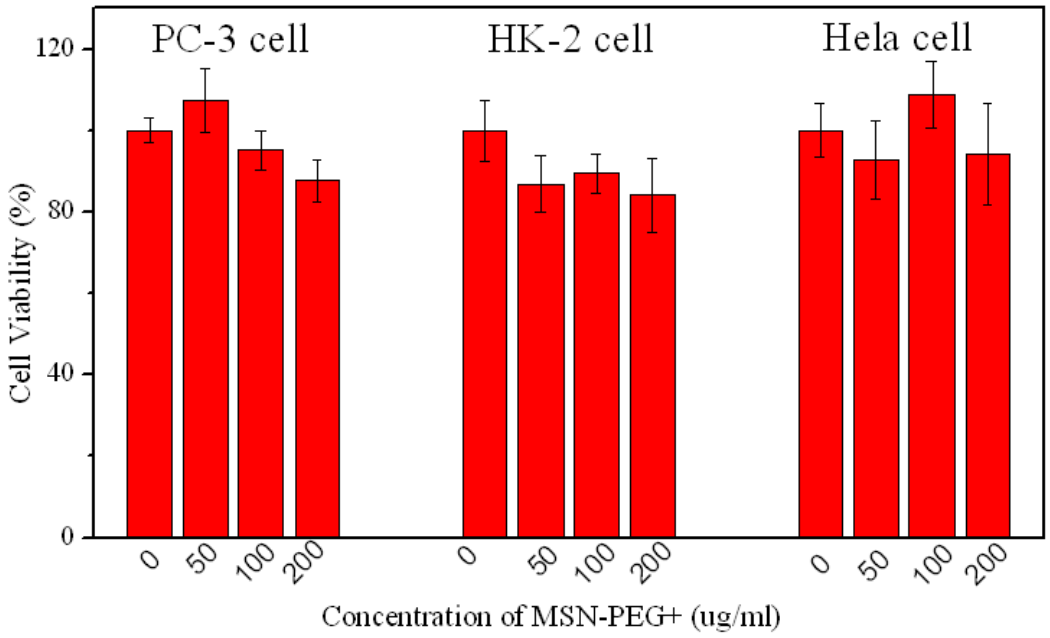


Figure S6. The viabilities of PC-3, HK-2 and Hela cells after incubation with MSN-PEG+ of different concentrations.

Parameter	Saline	MSN-PEG+	Parameter	Saline	MSN-PEG+	Parameter	Saline	MSN=PEG+
ALT(μL)	56.73±8.54	50.69±8.54	WBC(10^9/L)	4.57±1.19	4.43±1.24	MCV(fL)	45.77±2.16	45.33±1.47
AST(μL)	32.31±6.38	39.33±8.37	RBC(10^{12}/L)	9.41±0.46	9.44±0.56	MCH(pg)	15.40±0.35	15.27±0.36
BUN(mg/dL)	7.20±2.15	6.81±1.28	HGB(g/L)	144.67±6.77	151.67±7.03	MCHC(g/L)	336.33±9.25	336.66±5.20
Cr(mg/dL)	75.43±9.62	84.23±10.22	HCT (%)	43.05±2.77	45.05±1.83	PDN (%)	22.03±0.72	22.98±0.87

Table S1. The blood biochemistry and complete blood panel profiles of MSN-PEG+, containing blood urea nitrogen (BUN), white blood cells (WBC), mean corpuscular volume (MCV), creatinine (Cr), red blood cells (RBC), mean corpuscular hemoglobin (MCH), alanine aminotransferase(ALT), hemoglobin (HGB), mean corpuscular hemoglobin concentration (MCHC), aspartate aminotransferase(AST), hematocrit(HCT) and red cell distribution width (PDW).

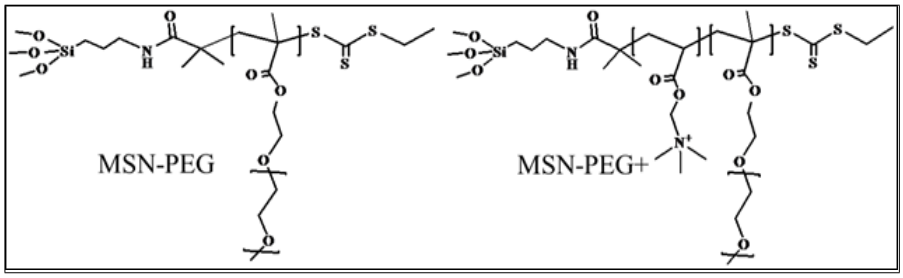


Figure S7.The chemical structure of MSN-PEG and MSN-PEG+

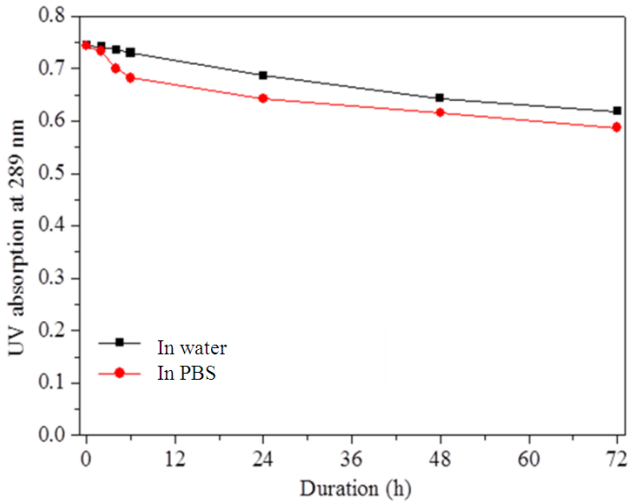


Figure S8. UV-vis absorption strength of MSN-PEG+ suspension at different time interval in water and saline solution, respectively, revealed that MSN-PEG+ can be maintained for more than 72 h without significant precipitation.

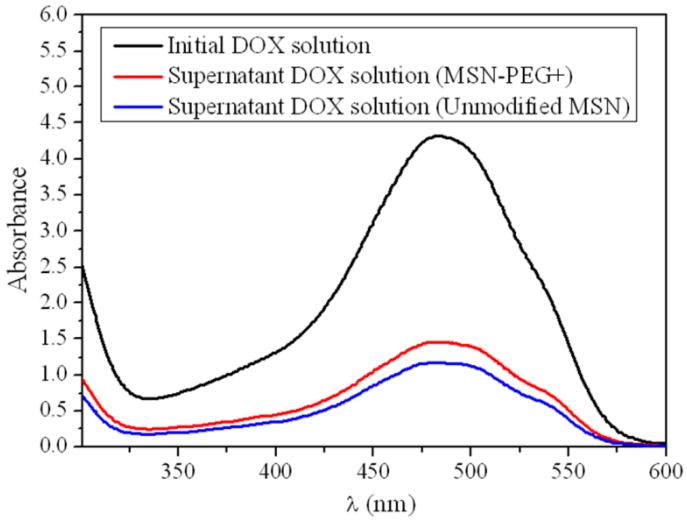


Figure S9. The UV spectra of initial DOX solution, supernatant DOX solution of MSN-PEG+ and unmodified MSN after centrifugation. The synthesized MSN-PEG+ exhibits a high drug loading capacity of about 25% and loading efficiency of about 66%, which is a little lower than the unmodified MSNs (Loading capacity: 27 %, loading efficiency: 73 %). This decrease in drug loading capacity and efficiency could be due to the inhibition of DOX adsorption on the outer surface of MSNs by PEG modification.

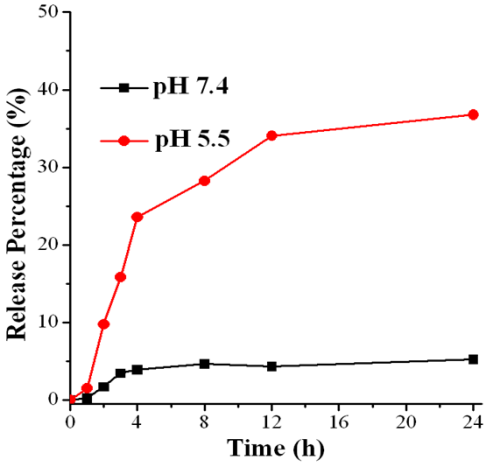


Figure S10. Drug release profiles of DOX-loaded MSN-PEG+ in pH 7.4 and pH 5.5.

Parameter	Saline	DOX loaded MSN-PEG+	Parameter	Saline	DOX loaded MSN-PEG+	Parameter	Saline	DOX-loaded MSN=PEG+
ALT(μL)	39.57±6.43	45.42±6.88	WBC(10^9/L)	13.14±1.56	11.57±2.18	MCV(fL)	50.70±0.92	50.69±1.40
AST(μL)	119.83±16.63	126.4±22.89	RBC(10^{12}/L)	8.50±0.33	8.37±0.48	MCH(pg)	16.30±0.48	16.27±0.45
BUN(mg/dL)	7.53±0.30	7.43±0.56	HGB(g/L)	138.43±3.60	136.14±7.60	MCHC(g/L)	321.57±5.47	321.00±2.24
Cr(mg/dL)	12.10±2.06	11.90±1.68	HCT (%)	43.07±1.41	42.44±2.62	PDN (%)	29.13±0.37	28.99±0.51

Table S2. The blood biochemistry and complete blood panel profiles of DOX loaded MSN-PEG+.

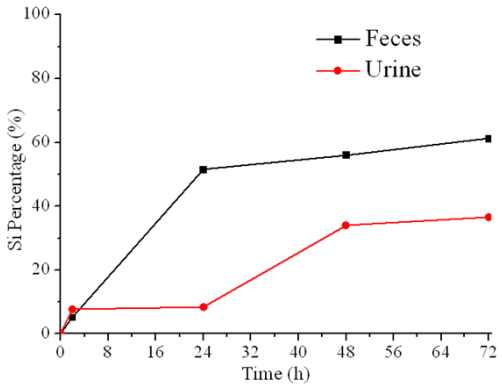


Figure S11. The cumulative amounts of Si detected in both urine and pieces before and after the injections of MSN-PEG+ nanoparticles at different time points (2, 24, 48 and 72 h).