Supporting information

METHODS

Preparation of BN nanotubes

The BNNTs were synthesized by a chemical vapor deposition method using boron and metal oxides as precursors. The detailed growth procedure was reported elsewhere. [1] The as-grown BNNTs were purified at ~ 1900 ^{o}C under the protection of Ar to remove impurities. Purified BNNTs were "snow-white" in color. The BNNTs were put in an alumina crucible and oxidized at 1000 ^{o}C for 5 h. The oxidized BNNTs were placed into a bottle with enough amount of water and ultrasonically dispersed for 5 h. Then they were filtered off after sonication and re-suspended in water at 25 μg/ml concentration.

Preparation of BNNT@mesoporous silica structure

In a typical synthesis, 50 mL of the mixture of BNNT suspensions, cetyltrimethyl ammonium bromide (CTAB) and sodium hydroxide (NaOH) was ultrasonically dispersed for about 2 h. The final concentrations of BNNT, CTAB and NaOH in the mixture were 20 μg/mL, 1 mg/mL and 0.001 mol/L, respectively. Certain amounts of tetraethylorthosilicate (TEOS, 0.111, 0.167 and 0.222 mmol) prediluted with ethanol in 1:4 proportion were added dropwise into the bottle, ultrasonically dispersed for about 5 min and treated at 60 ^{o}C for approximately 5 h. The obtained product was centrifuged, washed with water and ethanol for several times and re-dispersed in ethanol. The final product was named as BNNT@MS(-), BNNT@MS and BNNT@MS(+), respectively. In addition 0.222 mmol of a mixture of TEOS and 3-Aminopropyltrimethoxysilane (APTMS) in a molar ratio of 1.5:1 was used to prepare BNNT@MS-NH_2 using the same procedure.

Loading dox onto BNNTs

2 ml of BNNTs, BNNT@MS and BNNT@MS-NH_2 suspensions at 25 μg/ml in PBS solution (pH=5.7, 7.4, 9.0) and 100 μl of dox solution at 1 mg/ml in water were mixed and shaken at 200 rpm for about 16 h at room temperature. Then, the mixture was filtered through a 10kDa membrane and repeatedly filtered, and washed to remove free dox until the supernatant became nearly colorless.

Characterization

The morphology and structure observations were carried out by using a JEM-3000F transmission electron microscopy (TEM) operated at 300 kV. The nitrogen physisorption isotherms were recorded at 77 K on a Quantachrome Autosorb-1 system. Zeta potential was analyzed using a Delta Nano C Particle Analyzer (Beckman Coulter) by dispersing particles in 0.01M NaCl solution at the concentration of 2~3 μg/ml. Fourier transform infrared (FTIR) spectra were recorded using a Nicolet 4700 instrument by the KBr pellet method. Ultraviolet–visible (UV-vis) spectroscopy was used to record the dox concentration before and after loading. The amino groups were quantified by using 9-Fluorenylmethyl chloroformate (FmocCl) based on its complete protection of amino groups.

Then, piperidine was added for Fmoc cleavage and the ultraviolet absorption of supernatant Fmoc solution at λ =300 nm was measured for quantification analysis. [2]

LNcap prostate cancerous cell culture and incubation treatment

LNcap prostate cancerous cells with a cell density about 4×10^4 cells/cm^2 were cultured in 48-well plates containing RPMI1640 medium supplemented with 10% fetal bovine serum (FBS), 100 units/mL penicillin, and 100 mg/mL streptomycin at 37 ^{o}C in humidified air containing 5% CO_2. After overnight, BNNT, BNNT@MS and BNNT@MS-NH_2 suspensions loaded with dox were added into the above wells at a final concentration of 0.1, 0.25, 0.5, 1.0, 2.5, 5.0 μg/ml, respectively. After incubation for 5 h, the internalized dox was extracted by adding 10% Triton X-100 and 1M HCl acidified isopropanol and quantified fluorometrically (λ_{ex}=485 nm, λ_{ex}=570 nm).[3] The linear curve of dox concentration versus fluorescence intensity was obtained (Fig. S7). The internalization and release of the dox loaded onto nanotubes were directly imaged by fluorescence microscope (Leica DFC300FX). After incubation for 24 h, the culture medium in all wells was changed with fresh medium. The LNcap prostate cancerous cells viability were checked using a CCK-8 kit (Dojindo Molecular Technologies, Japan) in accordance with the manufacturer's instructions.

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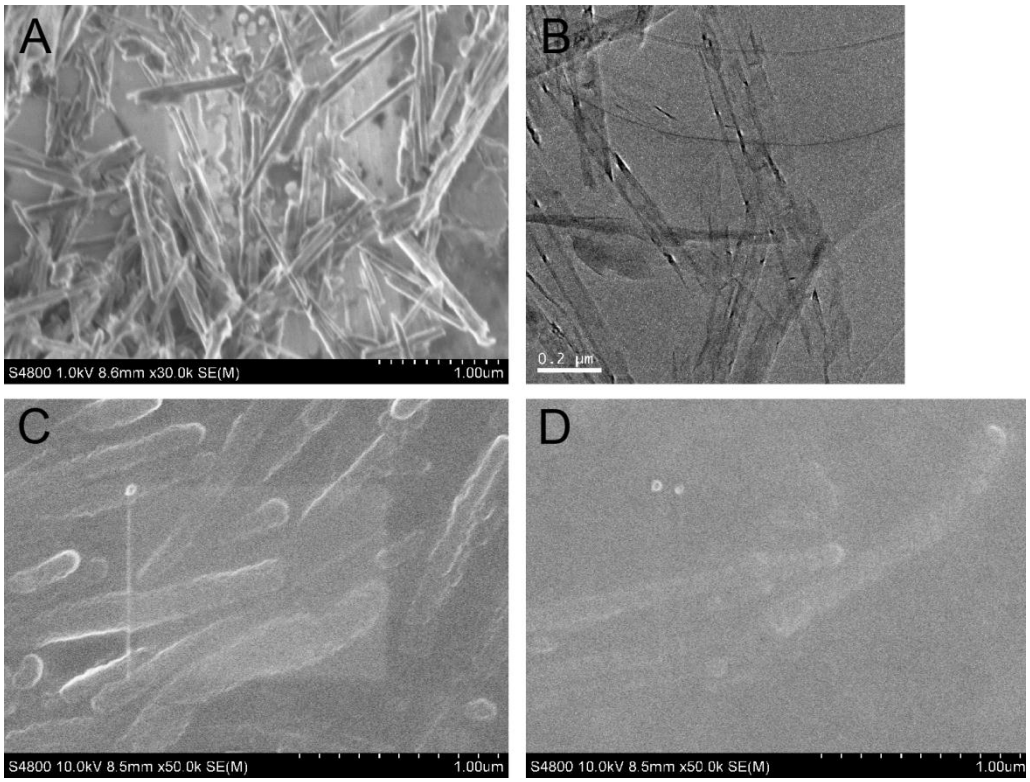

Fig S1. SEM (A) and TEM (B) images of BNNT; SEM images of BNNT@ MS (C) and BNNT-MS-NH_2 (D).

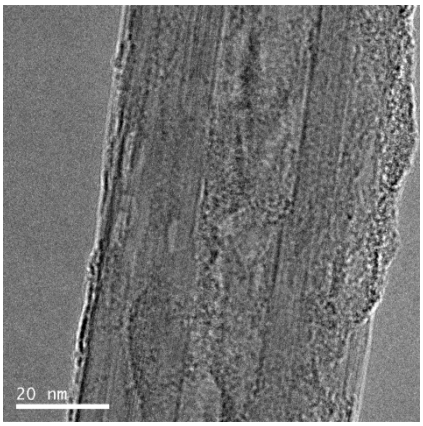

Fig S2. TEM image of a hydrogen peroxide BNNT @ MS hybrid.

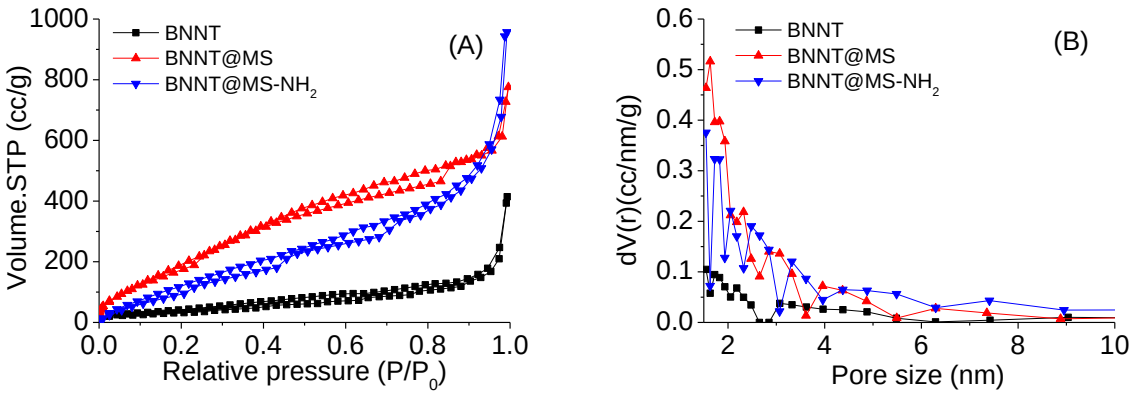

Fig S3. N_2 adsorption-desorption isotherms (A) and pore size distribution (B) of various samples.

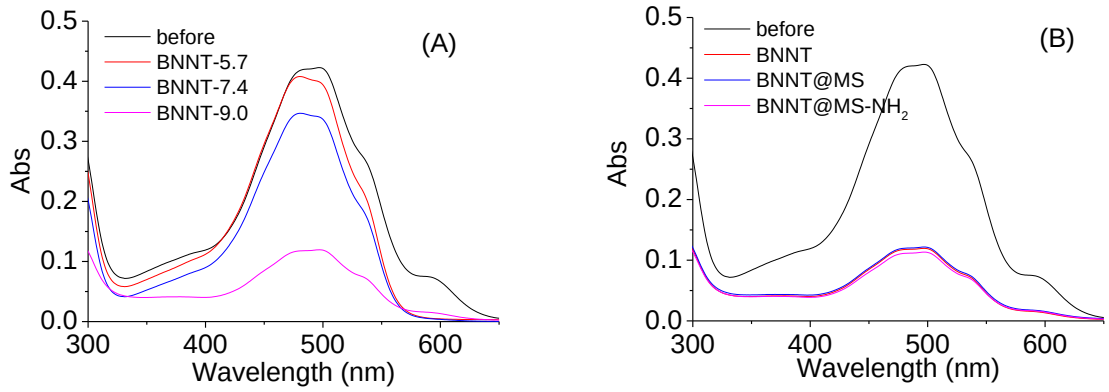

Fig S4. UV-vis spectra of dox solutions before and after loading on BNNT in PBS solution with different pH values of 5.7, 7.4 and 9.0 (A); UV-vis spectra of dox solutions in PBS solution (pH=9.0) before and after loading on BNNT, BNNT@MS and BNNT@MS-NH_2 samples, respectively (B).

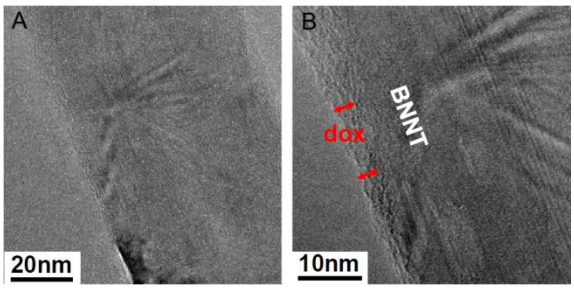

Fig S5. Low- (A) and high- (B) magnification TEM images of BNNTs loaded with dox.

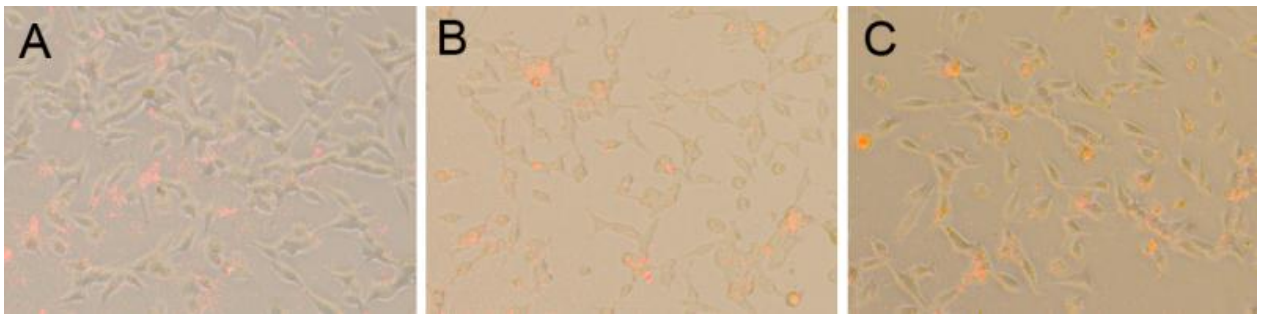

Fig S6. Fluorescence microscopy images of LNcap prostate cancer cells after culturing with the medium containing 1.0 μg/mL of BNNTs (A), BNNT@MS (B) and BNNT@MS-NH_2 (C) loaded with dox at 37°C for 5 h.

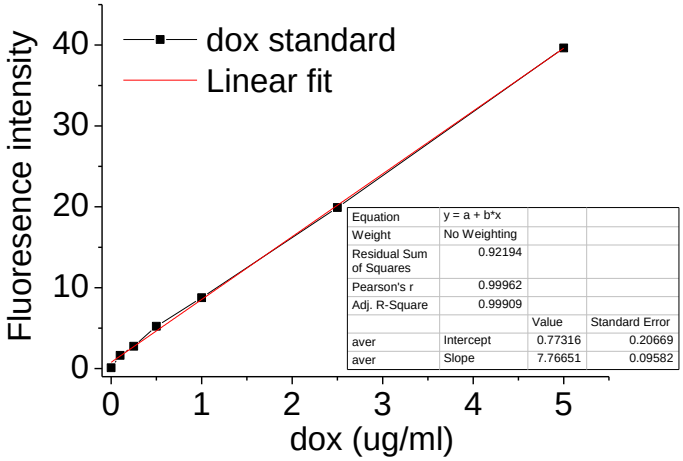

Fig S7. The linear curve of dox concentration versus fluorescence intensity.

References

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2 L. Q. Xiong, Z. G. Chen, M. X. Yu, F. Y. Li, C. Liu and C. H. Huang, *Biomaterials*, 2009, **30**, 5592-5600.

3 K. M. Laginha, S. Verwoert, G. J. Charrois and T. M. Allen, *Clin. Cancer. Res.*, 2005, **11**, 6944-6949.