Supplementary Information for

ORIGINAL ARTICLE

Transformative hyaluronic acid-based active targeting supramolecular nanoplatform improve long circulation and enhance cellular uptake in cancer therapy

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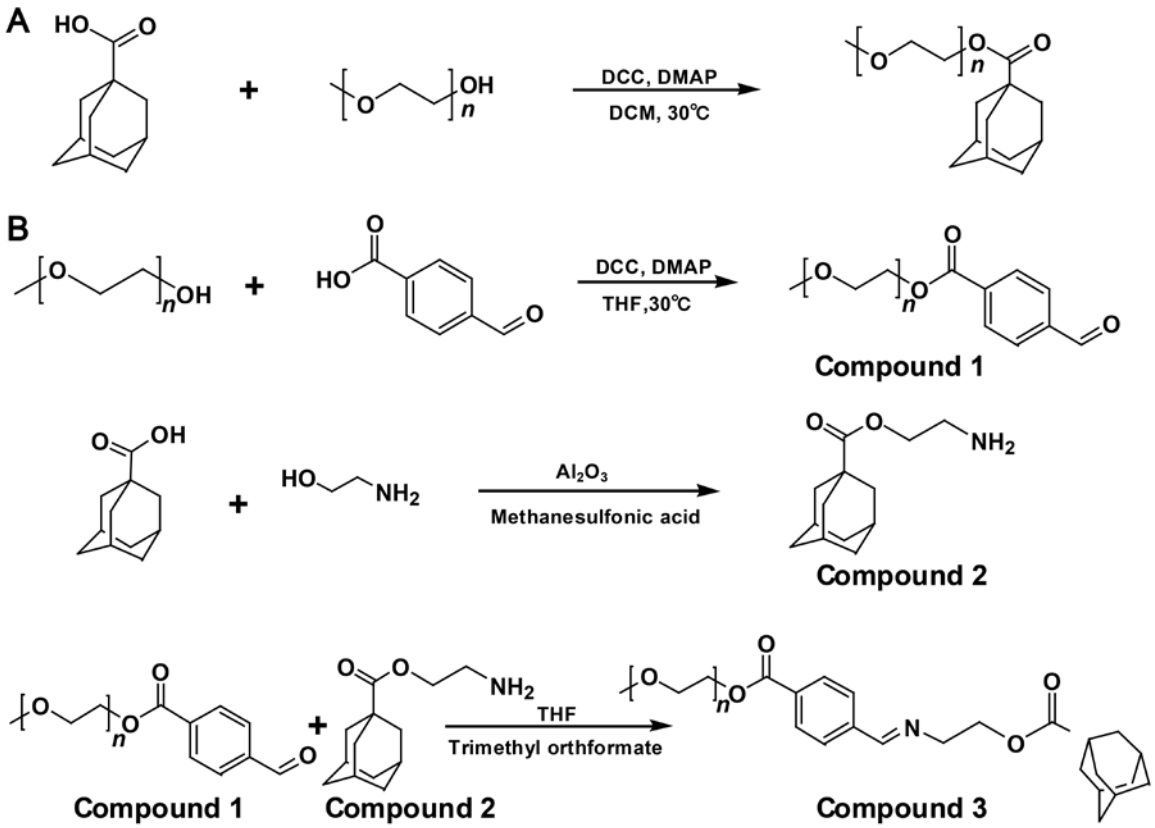

Scheme S1. Synthetic routes of pH sensitive AD-B-PEG (A) and non-pH sensitive AD-O-PEG (B).

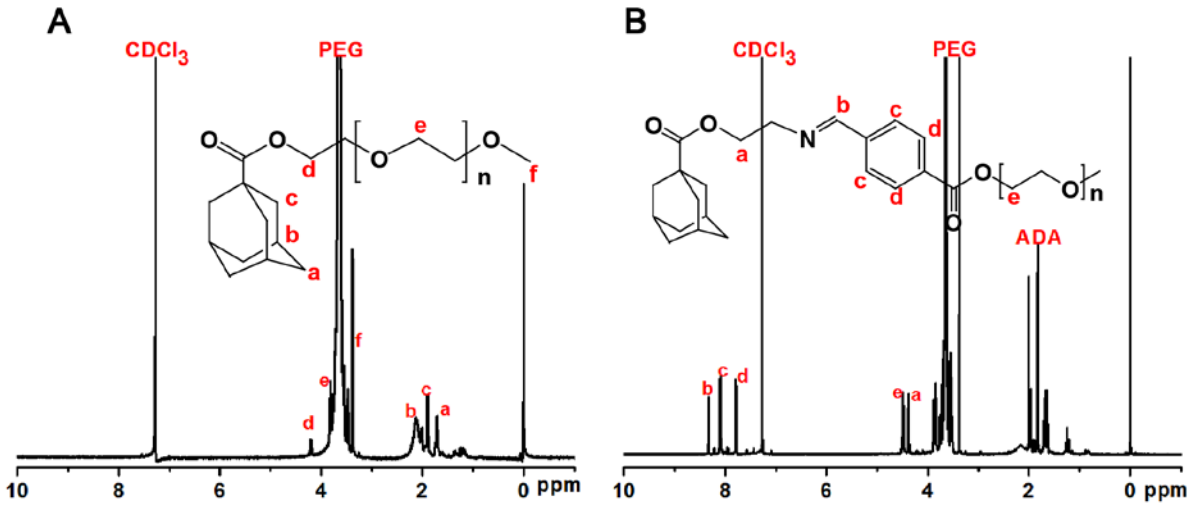

Figure S1. ^{1}H NMR spectra of AD-O-PEG (A) and AD-B-PEG (B) in $CDCl_3$.

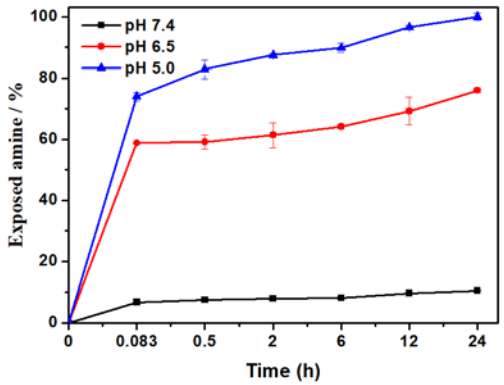

Figure S2. Hydrolysis of AD-B-PEG at different pH values.

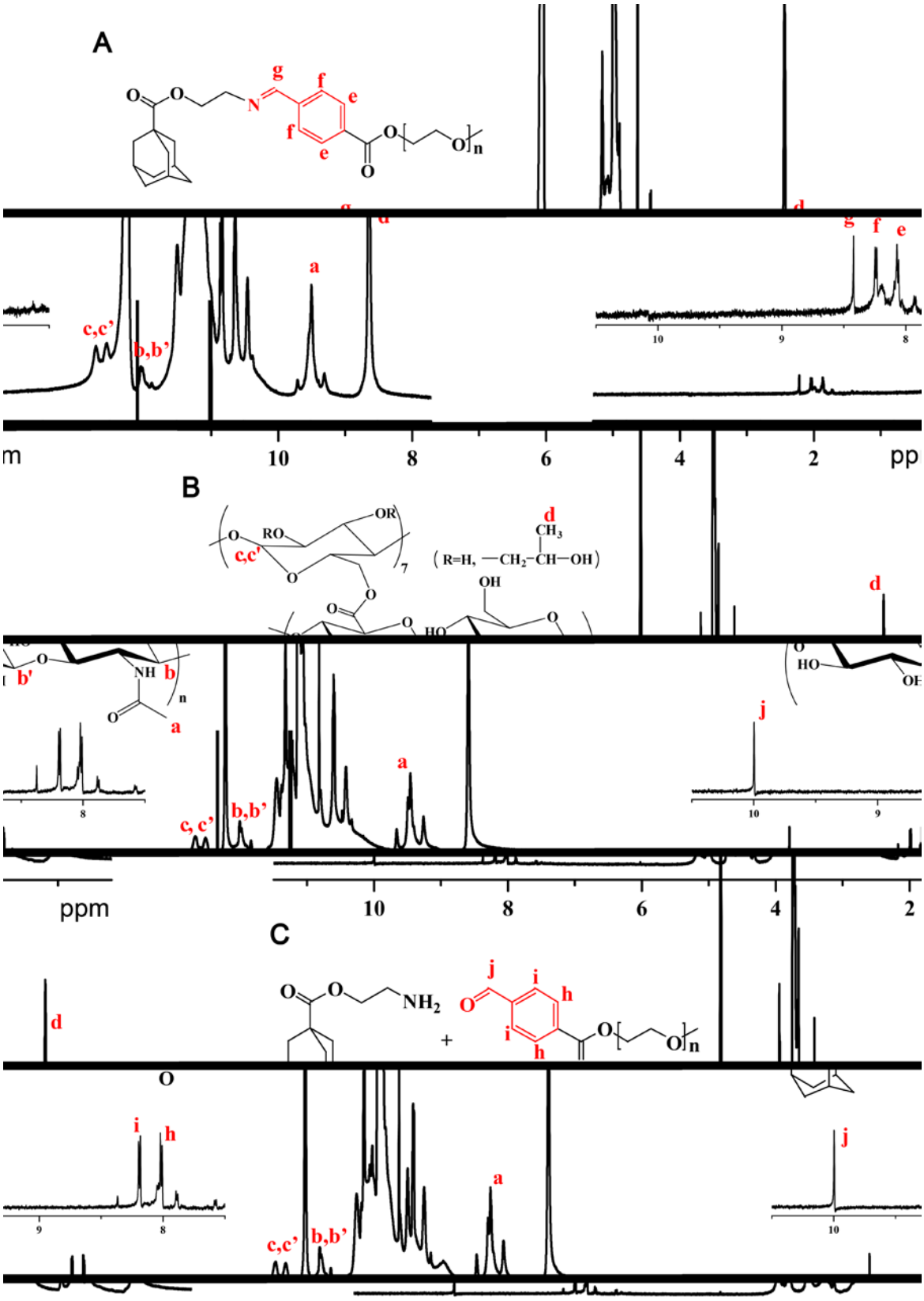

Figure S3. ^{1}H NMR spectra of HCBP in D_2O at pH 7.4 (A), 6.5 (B) and 5.0 (C). The samples were analyzed after being dissolved in D_2O at the desired pH values for 30 min.

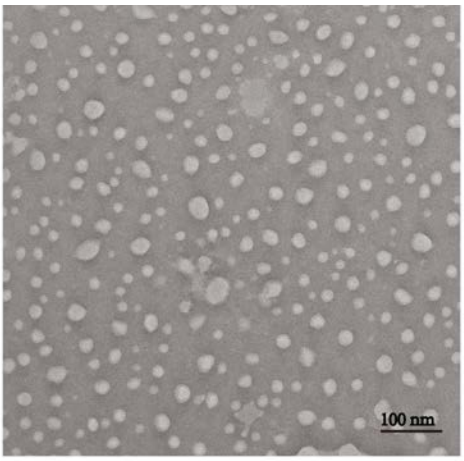

Figure S4. The observation of sample prepared with pH 7.4 HEPES buffer solution by TEM.

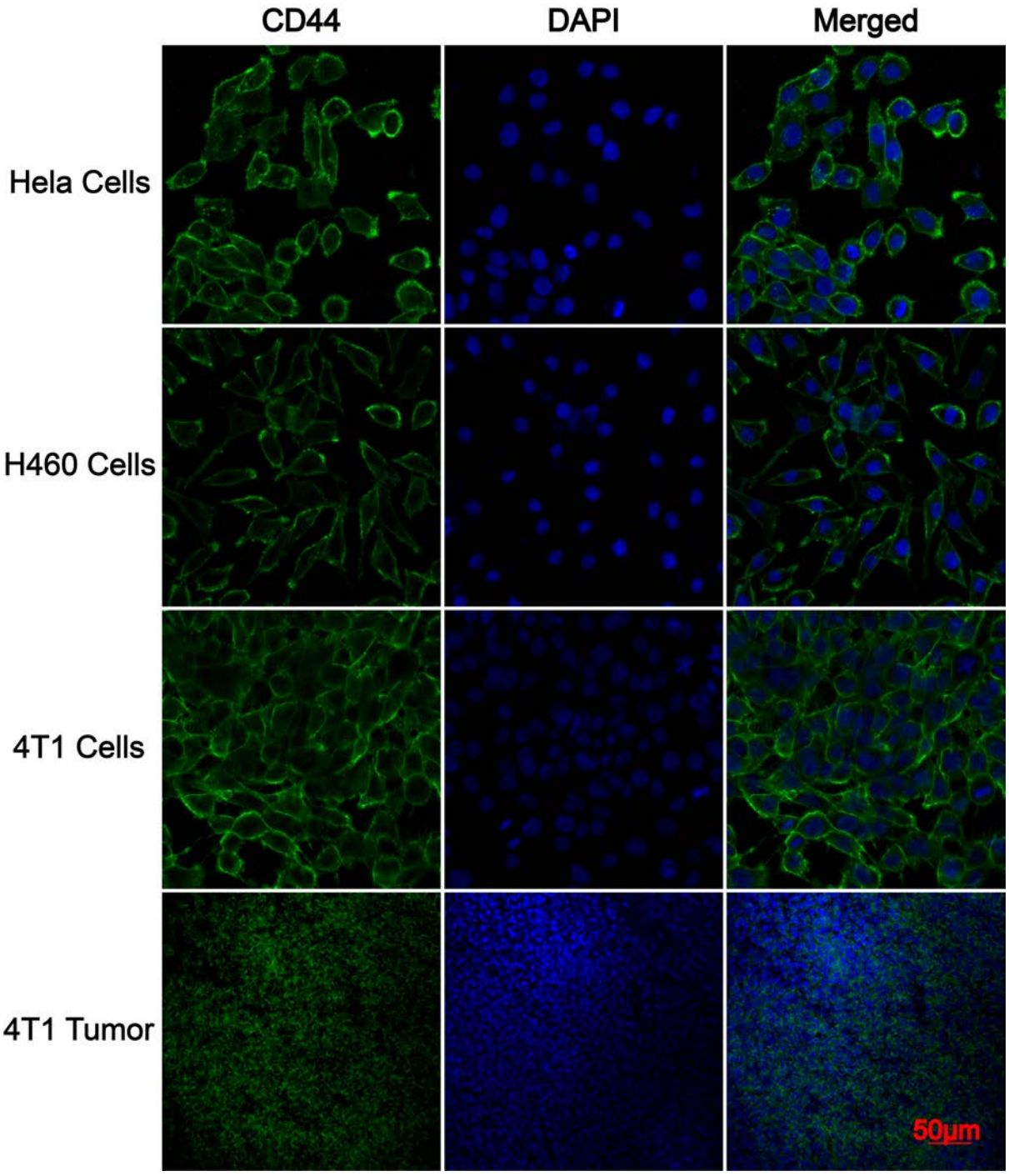

Figure S5. Analysis of CD44 receptor expression by immunofluorescence image with CLSM on various tumor cells and 4T1 tumor tissue.

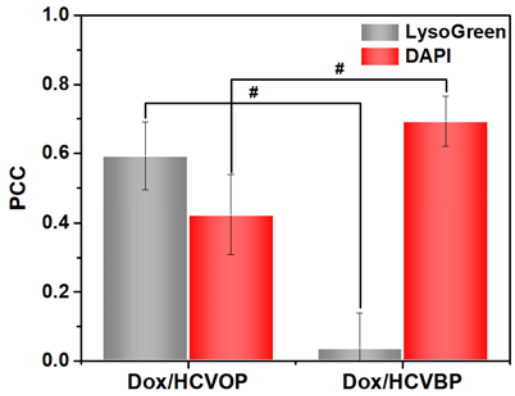

Figure S6. Pearson's correlation coefficient (PCC) of Dox/HCVPs comparing the overlap of Dox with LysoGreen (endo/lysosomes) and DAPI (nucleus) based on results of CLSM at 5 h.

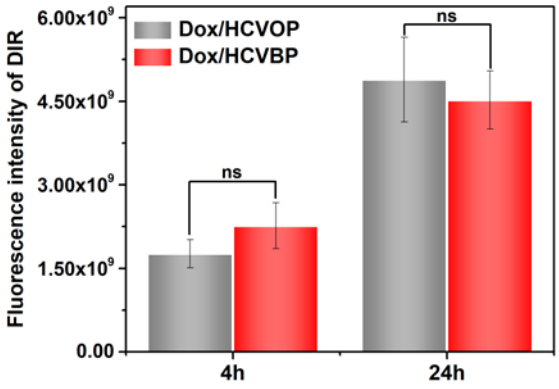

Figure S7. Average fluorescence intensity of DIR in tumor tissues of 4T1 bearing mice was semiquantificationally analyzed at 4 and 24 h after administrated DIR/HCVPs (n = 3).

Table S1. Physiochemical and pharmaceutical characteristics of Dox/HCVPs. Data were shown as mean ± standard deviation (mean ± SD, n=3).

Nanoparticle	Size	PDI	zeta	EE%	DL%
Dox/HCVOP	140.9±3.329	0.088±0.078	-28.8±0.950	94.25±3.30	2.61±0.13
Dox/HCVBP	139.8±3.835	0.109±0.029	-28.1±0.379	93.51±2.29	2.72±0.17

Table S2. IC_{50} values (nM) of Dox, Dox/HCVPs on Hela and H460 cells for 48 h incubation.

Cell	Dox	Dox/HCVOP	Dox/HCVBP
Hela	37.53	75.03	41.86
H460	397.70	376.10	179.10

Table S3. Pharmacokinetic parameters of Dox and Dox/HCVPs in rats after a single intravenous administration at the dose of 5 mg/kg (n = 5).

parameter	Dox	Dox/HCVOP	Dox/HCVBP
AUC_{0-t} (μg/L·h)	1034.722±305.868	4462.387±1001.992	3931.593±770.229
$AUC_{0-\infty}$ (μg/L·h)	1342.99±255.282	6572.503±1281.028	5613.767±1301.930
$t_{1/2}$ (h)	29.288±3.104	102.368±28.611	101.641±14.904