Supporting Information for

Anisamide-Decorated pH-Sensitive Degradable Chimaeric Polymersomes Mediate Potent and Targeted Protein Delivery to Lung Cancer Cells

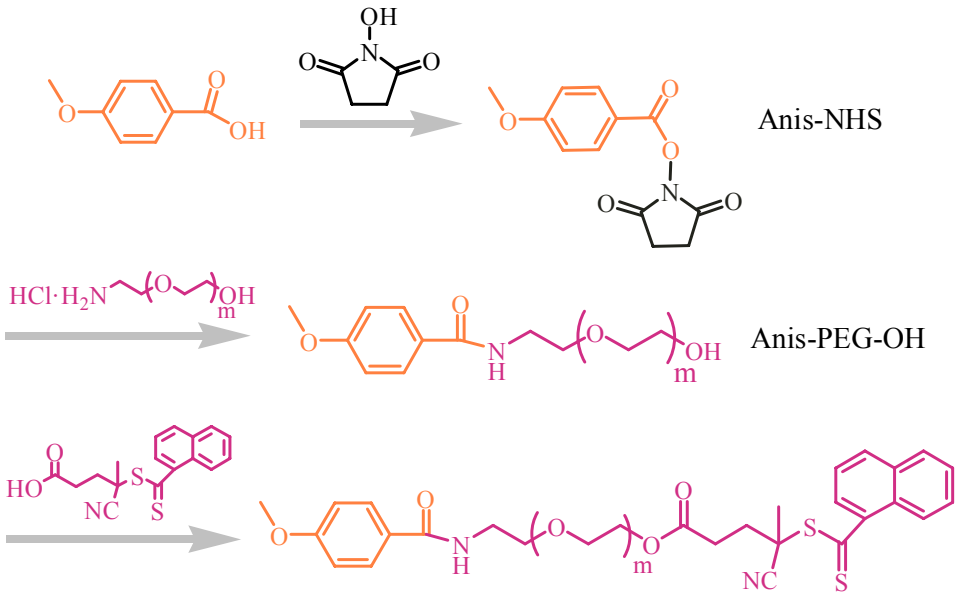
Ling Lu, Yan Zou, Weijing Yang, Fenghua Meng*, Chao Deng, Ru Cheng, and Zhiyuan Zhong*

Biomedical Polymers Laboratory, and Jiangsu Key Laboratory of Advanced Functional Polymer Design and Application, College of Chemistry, Chemical Engineering and Materials Science, Soochow University, Suzhou, 215123, P. R. China.

* Corresponding authors. Tel/Fax: +86-512-65882060, Email: fhmeng@suda.edu.cn (F. Meng); zyzhong@suda.edu.cn (Z. Zhong)

Synthesis of Anis-NHS

Briefly, to a THF solution (70 mL) of *p*-anisic acid (3.04 g, 20.0 mmol) and NHS (2.76 g, 24.0 mmol), a solution of dicyclohexyl carbodiimide (DCC, 4.96 g, 24.0 mmol) in THF (30 mL) was added dropwise at room temperature (r.t.) under constant stirring. After completing the addition of DCC, the reaction was allowed to proceed for 12 h. The mixture was analyzed via thin-layer chromatography, and nearly quantitative conversion of *p*-anisic acid to Anis-NHS was observed. The product was filtered to remove the precipitate, and the filtrate was concentrated using rotary evaporator. Anis-NHS was purified by crystallization from 2-propanol. Yield: 90 %. ^{1}H NMR (400 MHz, $CDCl_3$, Figure S1A): δ 8.08 (d, 2H), 6.96 (d, 2H), 3.69 (s, 3H), 2.89 (s, 2H).



Scheme S1 Synthesis of Anis-PEG-CPADN maro-RAFT agent. Conditions: (i) DCC, NHS, THF, r.t. 12 h; (ii) Et_3N, DCM, 25 °C, 24 h; (iii) DCC, DMAP, DCM, 25 °C, 24 h.

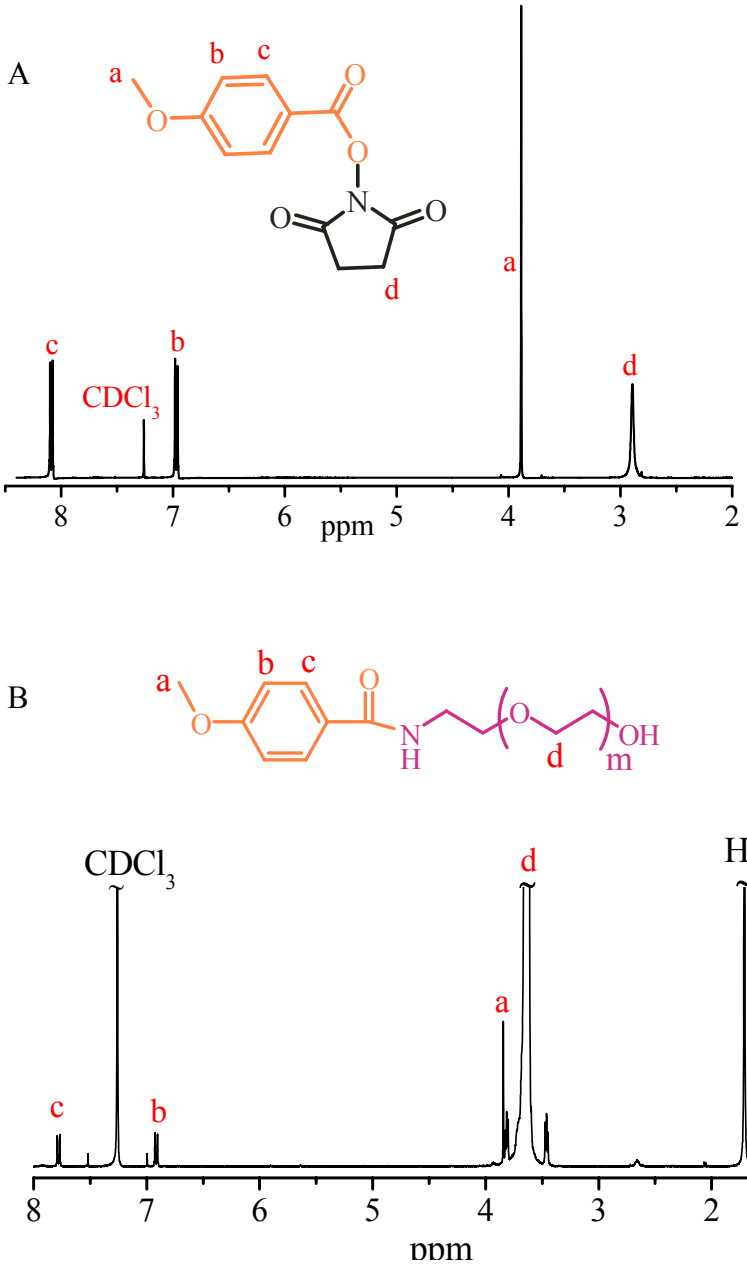


Fig. S1 ^{1}H NMR spectra (400 MHz, $CDCl_3$) of Anis-NHS (A) and Anis-PEG-OH (B).

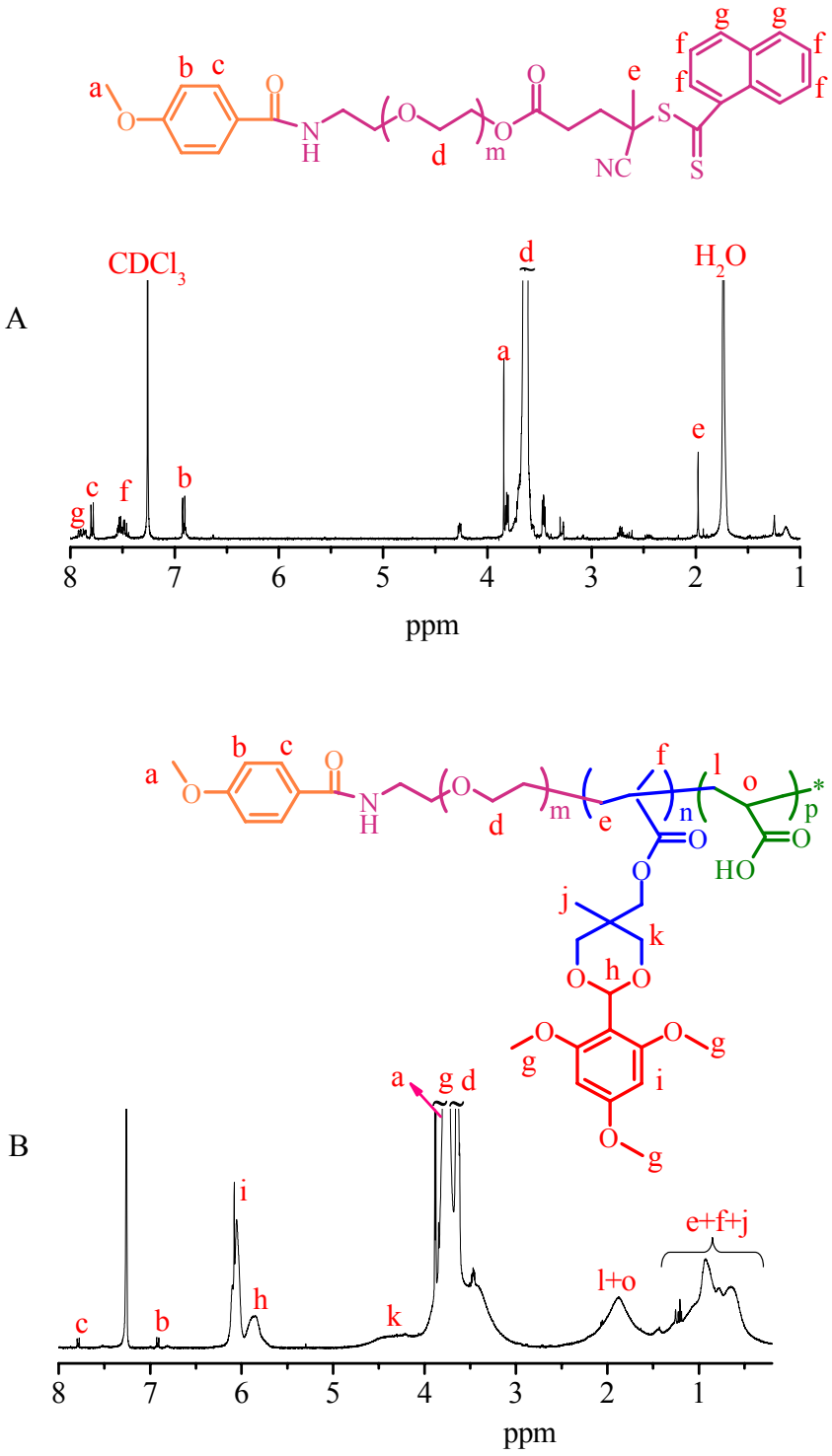


Fig. S2 ^{1}H NMR spectra (400 MHz, $CDCl_3$) of Anis-PEG-CPADN (A) and Anis-PEG-PTTMA-PAA (B).

Table S1 Characteristics of GrB-AnisX-CPs (feed ratio of 0.4 wt.%)

Entry	Polymersomes	Size (nm) [a]	PDI [a]	ζ (mV) [b]	IC_{50} (μg/mL)	
					H460	PC-3
1	GrB-CPs	138	0.11	0.40±0.2	1.24	-
2	GrB-Anis20-CPs	145	0.04	0.65±0.2	1.05	-
3	GrB-Anis30-CPs	146	0.06	0.73±0.3	1.02	0.77
4	GrB-Anis50- CPs	155	0.04	0.68±0.1	0.66	0.40
5	GrB-Anis70- CPs	166	0.01	0.92±0.4	0.20	0.19
6	GrB-Anis80- CPs	169	0.04	0.95±0.3	0.12	-
7	GrB-Anis100- CPs	179	0.01	0.98±0.2	0.87	-

[a] Determined at 25 °C with a Zetasizer Nano ZS instrument (Malvern) equipped with a dynamic light scattering (DLS, 10 mW He-Ne laser, 633 nm wavelength) in PB buffer (pH 7.4, 10 mM).

[b] Determined at 25 °C with a Zetasizer Nano ZS instrument (Malvern) equipped with a standard capillary electrophoresis cell in PB buffer (pH 7.4, 10 mM).

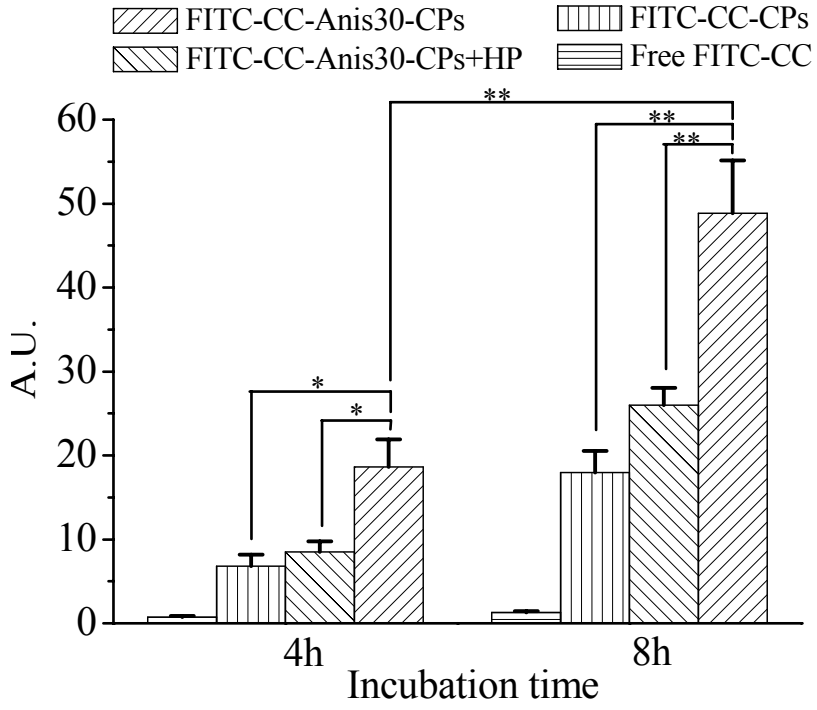


Fig. S3 The relative green fluorescence intensity in H460 cells according to the CLSM images (Figure 8). Each value was the average selection from 20-25 H460 cells (Student's *t* test, $*p < 0.05$, $**p < 0.01$).

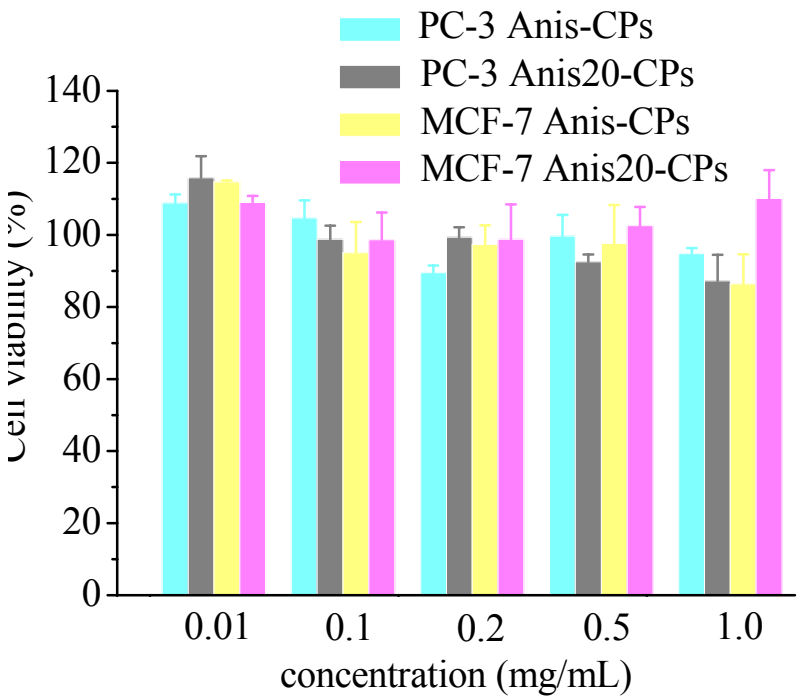


Fig. S4 Cytotoxicity of CPs and Anis20-CPs toward PC-3 and MCF-7 cells following 48 h incubation determined by MTT assays. Data are shown as mean ± SD (n = 4).

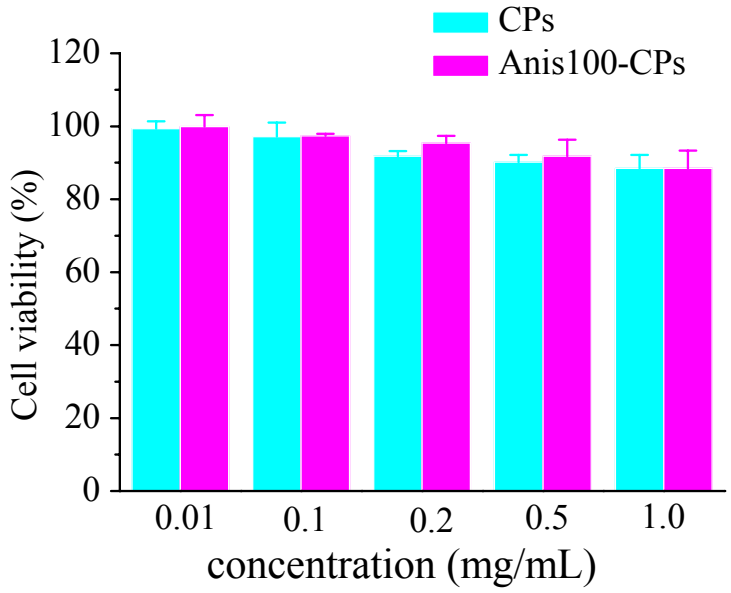


Fig. S5 Cytotoxicity of CPs and Anis100-CPs toward H460 cells following 24 h incubation determined by MTT assays. Data are shown as mean ± SD (n = 4).