Supplementary Information

Hydrogels formation: 2.5 mg compounds were dissolved in 0.2 mL PBS solution containing 6 equiv. of Na_2CO_3 (0.1mol/L). 2 equiv. of Na_2CO_3 were used to neutralize the compounds and the additional 4 equiv. of Na_2CO_3 were used to neutralize GSH. 0.10 mL PBS solution containing 4 equiv. of GSH (1 mg/mL) was added. Hydrogels would form after being kept at room temperature for less than 10 minutes.

The morphological characteristics of hydrogels: Nano ZS90 Zetasizer (Malvern Instruments, Britain) was used to measure the Zeta potential of the hydrogels by dynamic light scattering. Transmission electron microscopy (TEM) samples were performed on a JEM-2100 electron microscope. The sample powder was deposited on a copper stub and the images were taken by S-4800 Scanning Electron Microscope (SEM).
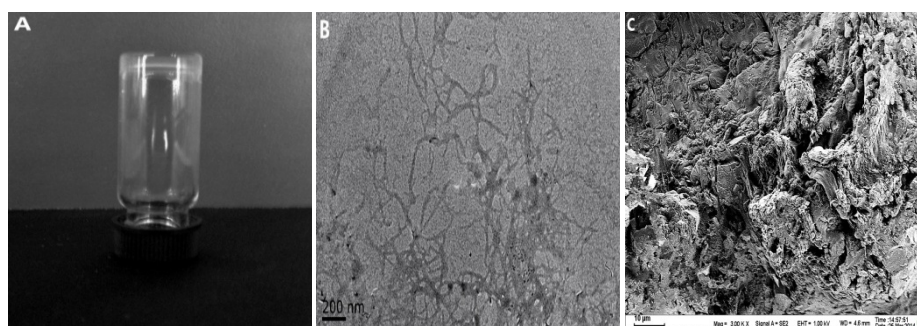

Figure S-1. Optical (A), TEM (B) and SEM images (C) of the Et-peptide-Taxol hydrogel.
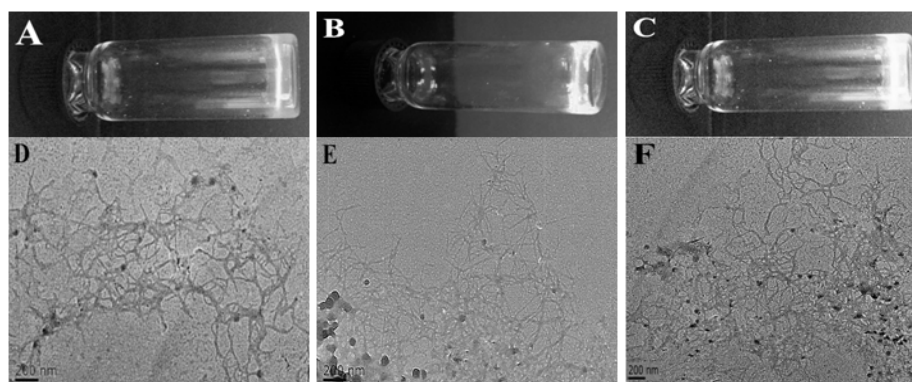

Figure S-2. Optical images (A-C) and the corresponding TEM images (D-F) of the control carrier (A, D), non-targeting (B, E) and single-targeting (C, F) hydrogels.

Rheology: The dynamic strain sweep and dynamic frequency sweep were performed on an AR 2000ex (TA instrument, America) system. A dynamic strain sweep was performed to ensure the linear region of dynamic viscoelasticity at the frequency of 6.28 rad/s and temperature at 25℃. The hydrogel was characterized by the mode of dynamic frequency sweep in the region of 0.1–100 rad $^{s-1}$ at the strain of 1%.
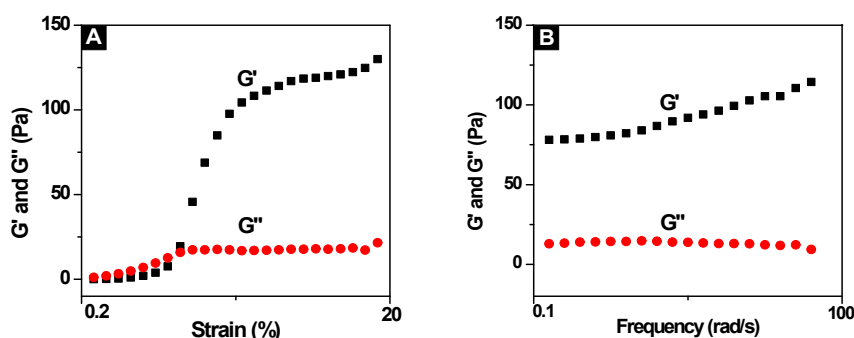
Figure S-3. The strain (A) and frequency (B) dependence of dynamic storage modulus G' and loss modulus G'' of the hydrogel.

Release profile: The hydrogels in PBS (pH = 7.4) solution containing different concentration (1.0 wt%, 1.2 wt%, 1.5 wt %) were formed at 37 °C for 24 h. Then 0.25 mL of PBS was added on the surface of hydrogels. For the following time points, 0.2 mL of PBS solution was taken out and 0.2 mL of fresh PBS solution was added back at each point. The release profile of free Taxol from the gel was monitored by HPLC (Shimadzu, Japan) system. The detection wavelength was 227 nm and the experiment was performed at least three times.

In order to have an approximate idea about the probable mechanism of the Taxol release from the hydrogels, the release data were analyzed according to the empirical Ritger-Peppas equation：

$$M_t / M_\infty = k \cdot t^n \qquad (1)$$

Where M_t / M_∞ is fractional drug release, M_t is the amount of drug released at time t, M_∞ is the maximum amount of drug released at time ∞, t is the release time, k is a rate constant of kinetic release, and n is the diffusion exponent, characteristic of the drug release mechanism. For n< 0.5, it indicates that the drug release follows the Fickian diffusion, whereas the non Fickian drug release process has a value of n between 0.5 and 1.

Determination of IC$_{50}$ values: The IC$_{50}$ values of *Et*-KYE-CS-E*RGD*-FFG (control carrier, Et-peptide), Et-peptide hydrogel, free Taxol, *Et*-K (Taxol) YE-CS-E*RGD*-FFG (Et-peptide-Taxol) and Et-peptide-Taxol hydrogel were evaluated by the MTT (3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide, Biosharp) assay. The MCF-7 cells (ATCC, America) were cultivated in RPMI-1640, plus 10% fetal bovine serum and maintained at 37℃ in 5% CO$_2$. The cells were seeded in 96-well plates at density of 2,000 cells per well with a total medium volume of 100 μL and incubated for 24 hours. Then 100 μL of the solutions containing a serial of concentrations of the above four samples were added into the cells and calculated for 48 hours. Then the medium was replaced with 20 μL MTT reagent (5 mg/mL). 4 hours later, DMSO (100 μL/well) was added to dissolve the formazan crystals. The optical density of the solution was measured at 490 nm using a microplate reader (Bio-RAD, America). Cells without the treatment were used as the control. The experiment was repeated for 3 times. The cell viability percent was calculated by the following formula:

$$\text{The cell viability percent (\%)} = \text{OD}_{\text{sample}} / \text{OD}_{\text{control}} * 100\% \qquad (4)$$

The concentrations of the compounds when 50% of cells viability was recorded represented the IC_{50} values of the compounds.

Preparation of ICG-hydrogel formulation: The indocyanine green (ICG) and compounds were placed in PBS solution and stirred at room temperature for 5 min according to the mass ratio 1:10. Then the solutions were filtrated using 2000 Da filters (Millipore) to remove excess nonbinding ICG. The result products were dissolved in PBS solution containing 6 equiv. of Na_2CO_3 (0.1mol/L) and 4 equiv. of GSH (1mg/mL). Hydrogels formed after being kept at room temperature for less than 30 minutes. The fluorescence analysis was performed on a RF-5301 spectrofluorimeter (Shimadzu, Japan), and the fluorescence spectra were recorded in the wavelength range of 400-900 nm upon excitation at 400 nm. The excitation and emission slit widths were 5 nm, and scan speed were kept constant with each data set. Each experiment was repeated at least three times and found to be reproducible within experimental errors. Confocal images of ICG and ICG-Hydrogel nanofibers in PBS solution were performed on a confocal microscope (Olympus IX71, Japan).
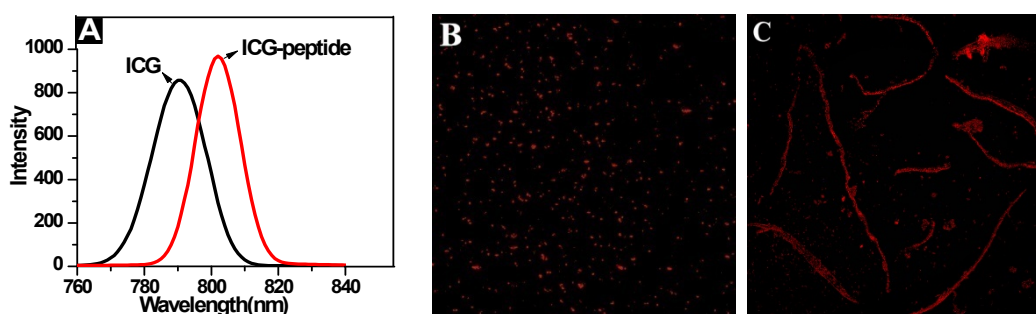

Figure S-4. Fluorescence emission spectra (A) of ICG and ICG conjugated with Et-peptide-Taxol precursor (ICG-peptide, excitation wavelength: 400 nm, excitation and emission slit widths: 5 nm). Confocal images of ICG（B）and ICG-Hydrogel nanofibers (C) in PBS solution (Bar: 100μm)

Cell imaging: The Nap-K (Taxol) YE-CS-ERGE-FFG (non-targeting), *Et*-K (Taxol) YE-CS-ERGE-FFG (single-targeting) and *Et*-K (Taxol) YE-CS-E*RGD*-FFG (dual-targeting) hydrogels conjugated with ICG were prepared for discussing the targeting and anticancer effect. The MCF-7 cells (ATCC, America) were seeded in 24-well microtiter plates for 24 hours. The hydrogels were added and the cells were incubated for 4 or 12 hours respectively at 37℃ and 5% CO_2. The human gastric carcinoma cell line SCG7901 cells (ATCC, America) were treated with Et-peptide-Taxol hydrogel for control group. Then washed three times with 37℃ pre-heated PBS and imaged on a confocal microscope (Olympus IX71, Japan).
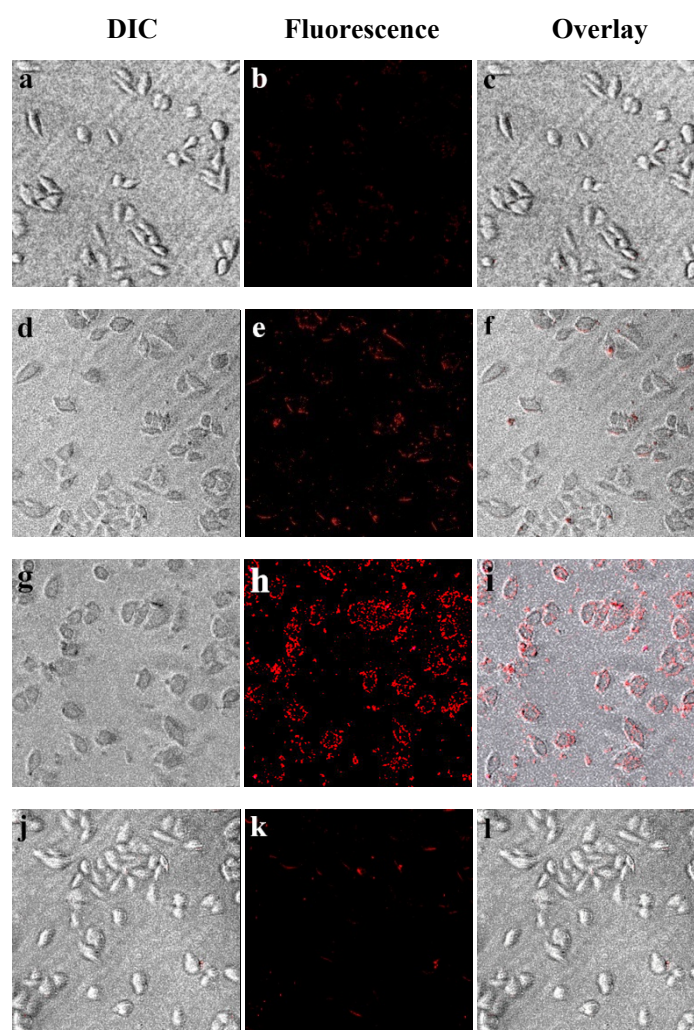
Figure S-5. Confocal images of MCF-7 cells after incubation with non-targeting （a-c）, single-targeting (d-e), dual-targeting hydrogels (g-i) and SCG7901 cells treated with dual-targeting hydrogel (j-l) for 4 hours after being washed by PBS solution (Bar: 100μm)

***In vivo* circulation and biodistribution studies:** Animals were treated according to the guidelines of the Committee on Care and animal experiments were approved by the Animal Care and Use Committee in China Pharmaceutical University. A nude mice model of human breast carcinoma xenografts (the tumor reached a size of about 0.2–0.3 cm^3, Key GEN Biotech. Co., China) was used for imaging *in vivo*. 200μL Et-peptide-Taxol hydrogel (1.0%) obtained was administered into nude mice via tail intravenously injection. A NIR imaging system which consists of an excitation light source (λ=765.9nm, NL-FC-2.0-763 laser light), a cold charge-coupled device (CCD) camera (PIXIS 512B, Princeton Instrument, America) was used for in vivo real-time fluorescence imaging.

Histological evaluation: To corroborate findings from the *in vivo* imaging, the animal used for detection of histopathology changes was sacrificed after one week. Briefly, animal was sacrificed by ether asphyxiation, and tissues were fixed in formalin for 2 days, following which it was processed by standard methods, embedded in paraffin, and sectioned. Samples were stained with hematoxylin-eosin (H&E) and were evaluated using a standard upright histology microscope

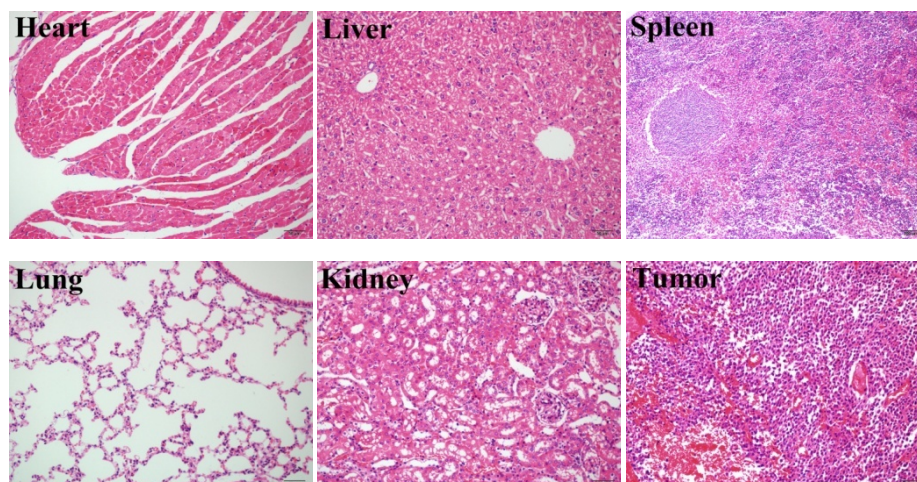(Olympus DX45, Japan) for notable histological observations.

Figure S-6. Histological analysis of vital organs (heart, liver, spleen, lung, kidney and tumor) treated with Et-peptide-Taxol hydrogel.

Estrone-succinyl N-hydroxysuccinimide (NHS) active ester[1-3] (Et-succi-NHS, yield of 64.5%): Estrone (0.1g, 0.37 mmol), succinic anhydride (0.074g, 0.74 mmol), triethylamine (TEA) (0.102ml, 0.74 mmol) and 4-(dimethylamino) pyridine (DMAP) (0.045g, 0.37 mmol) were dissolved in 10 ml of tetrahydrofuran (THF) and the reaction mixture was stirred overnight at 60°C. The solvent was evaporated under reduced pressure and then purified by column chromatography using methanol/DCM (1/20 v/v). The fractions were dried under vacuum. TLC, R_f =0.75 (methanol/DCM, 1:9).

The obtained product (0.037g, 0.1 mmol), N, N'-Diisopropylcarbodiimide (DIC) (20μL, 0.15 mmol) and NHS (0.017g, 0.15mmol) were dissolved in 10 ml THF with stirring for 4 hours at room temperature. The filtrate was removed under the reduced pressure and purified by column chromatography using ethyl acetate/toluene (1:4 v/v). The white active ester of the Estrone-succi-NHS was obtained after drying the fractions. The white product was then recrystallized from ethylacetate. TLC, Rf =0.68 (ethylacetate/toluene, 2:3); TOF-MS: m/z 490.2 [M+Na]. ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.16 (d, J = 8.4 Hz, 1H), 6.64 (d, J = 8.4 Hz, 1H), 6.59 (s, 1H), 2.92 – 2.81 (m, 2H), 2.51 (dd, J = 18.3, 8.4 Hz, 1H), 2.43 – 1.91 (m, 7H), 1.69 – 1.36 (m, 9H), 1.27 (s, 6H), 0.92 (s, 3H), 0.91 – 0.80 (m, 4H).
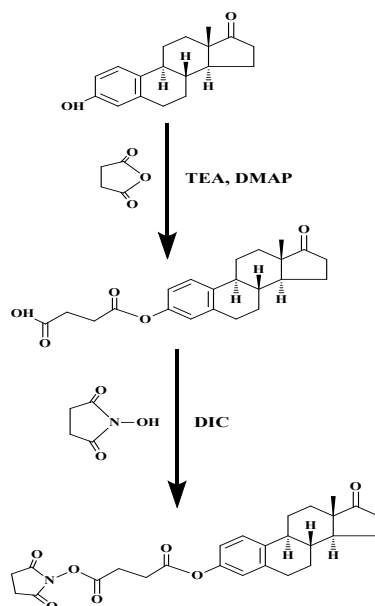
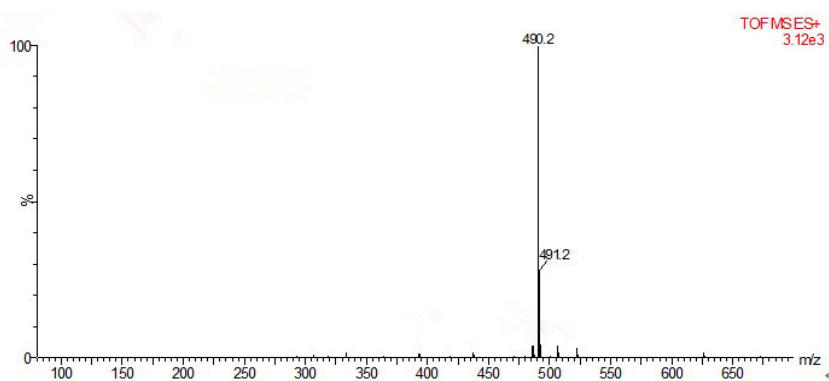**Scheme S-1**. Synthetic route for Et-succi-NHS active ester

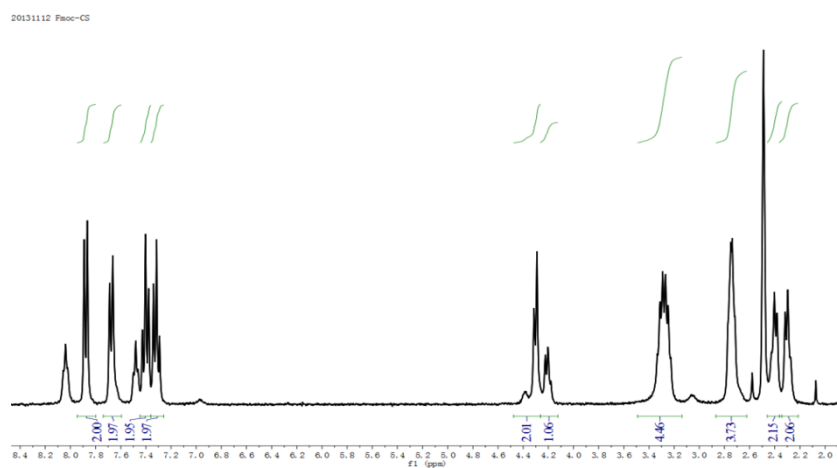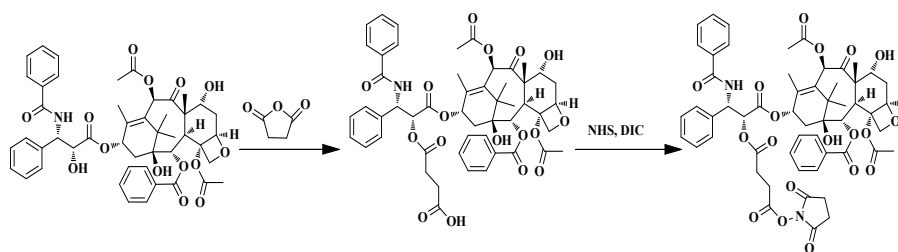**Figure S-7.** MS spectrum of Et-succi-NHS active ester

Figure S-8. ¹H NMR spectrum of Et-succi-NHS active ester

Taxol–succinyl N-hydroxysuccinimide (NHS) active ester[4-6] (Taxol-succi-NHS, yield of 92%):

Taxol (0.1708g, 0.2 mmol), succinic anhydride (0.07g, 0.7 mmol) and DMAP (0.0452g, 0.37 mmol) were dissolved in the 5 mL of dry pyridine by stirring for 3 hours at 25℃. The dry dichloromethane (DCM) was added into the above reaction mixture, and the organic phase was washed using 1 M HCl solution and water for three times respectively. The water phase was extracted by DCM. Combined the organic phase and washed by brine and dried over Na_2SO_4. The filtrate was concentrated on rotary evaporator and the crude product was used without further purification. The residue was dissolved in 5 mL of chloroform, and reacted with NHS (0.023g, 0.20 mmol) and DIC (35 μL, 0.2mmol) for 6 hours at 25℃. Purification with column chromatography (50:1 DCM/methanol) gave pure white product. TLC, Rf =0.68 (DCM / MeOH, 10:1). TOF-MS: m/z 1073.4 [M+Na]. ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.66 (s, 1H), 8.15 (d, J = 7.4 Hz, 2H), 7.85 − 7.67 (m, 1H), 7.66 − 7.21 (m, 11H), 7.20 − 7.01 (m, 1H), 6.34 − 6.11 (m, 2H), 6.05 − 5.91 (m, 1H), 5.68 (d, J = 7.1 Hz, 1H), 5.54 (t, J = 6.0 Hz, 1H), 4.98 (d, J = 9.1 Hz, 1H), 4.52 − 4.38 (m, 1H), 4.31 (d, J = 8.3 Hz, 1H), 4.21 (d, J = 8.3 Hz, 1H), 3.94 − 3.75 (m, 6H), 3.02 − 2.61 (m, 6H), 2.58 − 2.00 (m, 6H), 1.99 − 1.56 (m, 7H), 1.20 (dd, J = 29.8, 7.5 Hz, 35H).

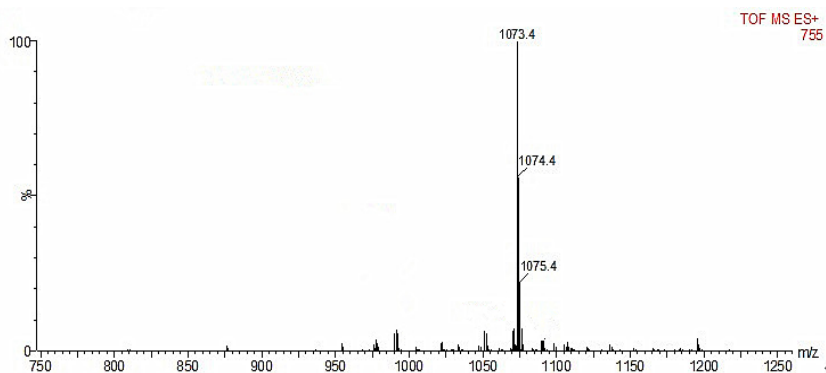**Scheme S-2**. Synthetic route for Taxol-succi-NHS active ester

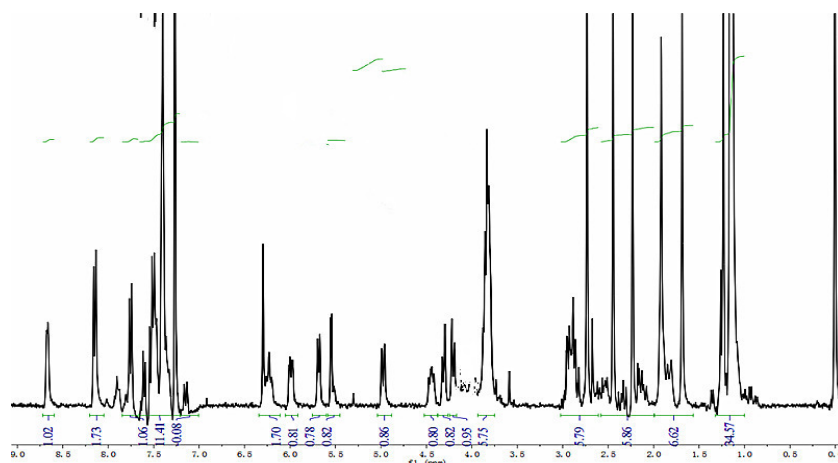**Figure S-9.** MS spectrum of Taxol-succi-NHS active ester

Figure S-10. ^{1}H NMR spectrum of Taxol-succi-NHS active ester

Synthesis of Disulfide Cleavable Linker[7-9] (Fmoc-CS, yield of 47.6%): The cystamine dihydrochloride (5 g, 22.2 mmol) and N, N-diisopropylethylamine (DIPEA, 7.7 mL, 44.4mmol) were added into methanol (25 mL). The mixture was cooled in an ice-water bath with a vigorous stirring for 30min. A succinic anhydride (2.22 g, 22.2 mmol) was added in 1, 4-dioxane (50 mL) over 60 min, and the resulting solution was stirred for 15 min at room temperature. After removed solvent under vacuum the aqueous Na_2CO_3 solution (2.6 g, 25 mmol) was added, and then the resulting solution was treated with ether (200 mL) to remove unreacted materials and side products. Collected the aqueous layer, followed by the addition of Na_2CO_3 (36 mmol, 3.8 g). The resulting solution was placed in an ice-water bath with a vigorous stirring to completely dissolute Na_2CO_3. Fmoc-OSu (7.4 g, 22.2 mmol) in 1, 4-dioxane was added dropwise over 60 min, and stirred at room temperature overnight. The filtrate was obtained by filtration and then concentrated to remove the solvent. 200 mL of ether was added into aqueous solution to remove the side products and unreacted materials. The aqueous layer was acidified with 1 M HCl to pH 1-2, and then extracted with DCM. The organic layer was dried over anhydrous Na_2SO_4 for 30 min and filtered. The solution was concentrated to a small volume and diluted with ether to give a white solid. Collected crystallized product, washed with ether, and dried in vacuum. A white solid powder was obtained. TOF-MS: m/z 513.1 [M+K]. ^{1}H NMR (300 MHz, DMSO) δ 7.88 (d, *J* = 7.4 Hz, 2H), 7.68 (d, *J* = 7.3 Hz, 2H), 7.40 (t, [10-12]*J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.1 Hz, 2H), 4.48 – 4.26 (m, 2H), 4.21 (d, *J* = 6.3 Hz, 1H), 3.28 (dd, *J* = 13.0, 6.3 Hz, 4H), 2.74 (d, *J* = 3.2 Hz, 4H), 2.39 (d, *J* = 6.1 Hz, 2H), 2.31 (d, *J* = 6.0 Hz, 2H).
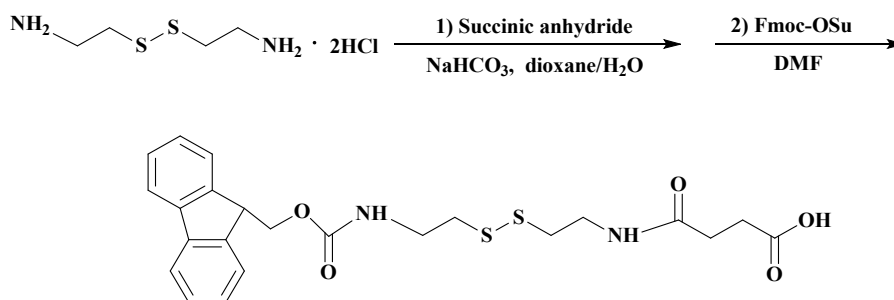
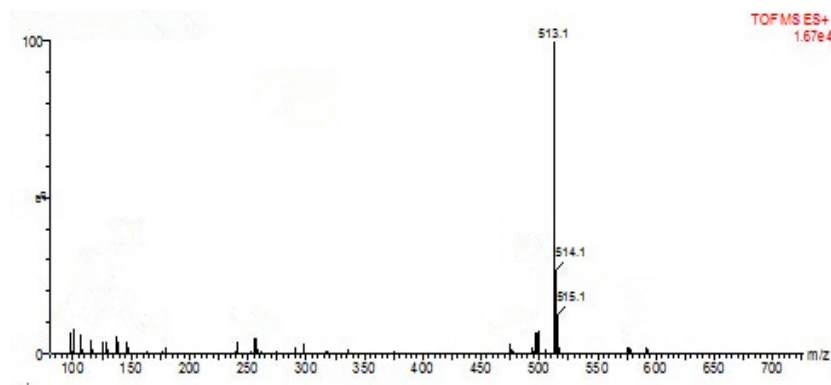

Scheme S-3. Synthetic route for Fmoc-CS compound

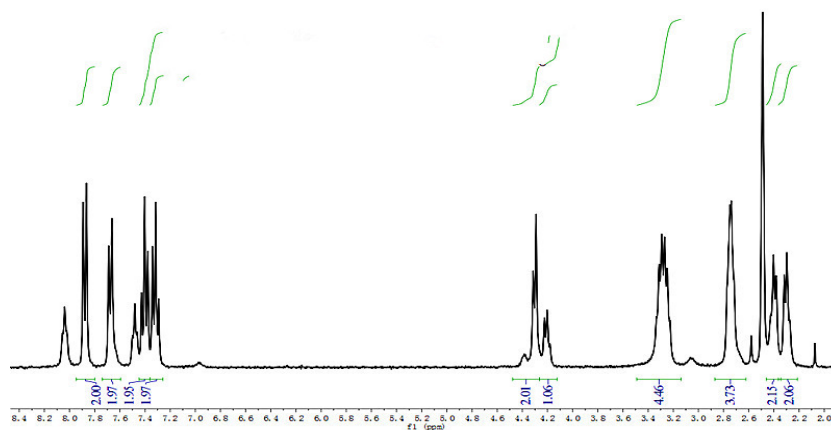**Figure S-11.** MS spectrum of Fmoc-CS compound

Figure S-12. ^{1}H NMR spectrum of Fmoc-CS compound

Peptide synthesis[13-15] (Fmoc-KYE-CS-ERGD-FFG, yield of 79.2%): The amino acid based hydrogel was prepared by the standard solid-phase peptide synthesis (SPPS), which used 2-chlorotrityl chloride resin (1.0~1.2 mmol/g) and N-Fmoc protected amino acids (GL Biochem, Shanghai, china). The resin was swelled in dry DCM for 20 minutes, and was washed with of dry DCM for three times. Then the first amino acid Fmoc-Gly-OH (2 equiv.) was loaded onto resin with adding DIPEA（2 equiv.) for 1 hour. After washed with DCM for three times, the unreacted sites in resin were quenched with blocking solution (80:15:5 of DCM/MeOH/DIPEA) for 20 minutes. Then the 20% piperidine (in DMF) was added for 30 min to remove the protecting group, followed by washing the resin in DMF for five times. Then conjugated the sequent Fmoc-protected amino acid (2 equiv.) to the free amino group using DIPEA / O-benzotriazole-N,N,N',N'-tetramethyl-uroniumhexafluoro-phosphate (HBTU) (2 equiv.) / 1-Hydroxybenzotriazole (HOBt) as the coupling reagent. These coupling and deprotection steps were repeated to elongate the peptide chain, which were carried out by the standard Fmoc SPPS protocol. Finally the resin was washed with DMF (5 times) and DCM (5 times) respectively. The peptide was cleaved from the resin by trifluoroacetic acid (TFA) and the mixture was stirred at room temperature for 1-2h. Filtered the resin and wash it 2 ~ 3 times with fresh TFA. The filtrate was concentrated on rotary evaporator and the crude product was poured into ice-cold ether. The resulting precipitate was centrifuged for 10 min at 13,000 rpm. Afterward the supernatant was dissolved in double-distilled water and lyophilized. The resulted crude products were purified by

reverse phase HPLC. TOF-MS: m/z 1704.0 [M⁺], 1705.0 [M+H]. ¹H NMR (300 MHz, DMSO) δ 8.44 – 8.02 (m, 12H), 8.02 – 7.18 (m, 36H), 7.18 – 6.94 (m, 8H), 6.71 (s, 1H), 6.64 (t, J = 9.8 Hz, 3H), 4.55 (s, 4H), 4.29 (dd, J = 36.5, 25.8 Hz, 9H), 4.23 (d, J = 5.1 Hz, 2H), 4.26 – 3.96 (m, 5H), 3.95 (s, 1H), 3.96 – 3.45 (m, 10H), 3.45 – 3.33 (m, 18H), 3.33 – 3.00 (m, 8H), 2.98 – 2.60 (m, 19H), 2.60 (s, 1H), 2.51 (d, J = 1.7 Hz, 6H), 2.46 – 2.14 (m, 13H), 2.14 – 1.91 (m, 2H), 1.91 (s, 1H), 1.90 (s, 2H), 1.80 (d, J = 39.3 Hz, 5H), 1.70 – 1.19 (m, 14H), 1.09 (t, J = 7.0 Hz, 22H), 0.87 (d, J = 7.1 Hz, 1H).
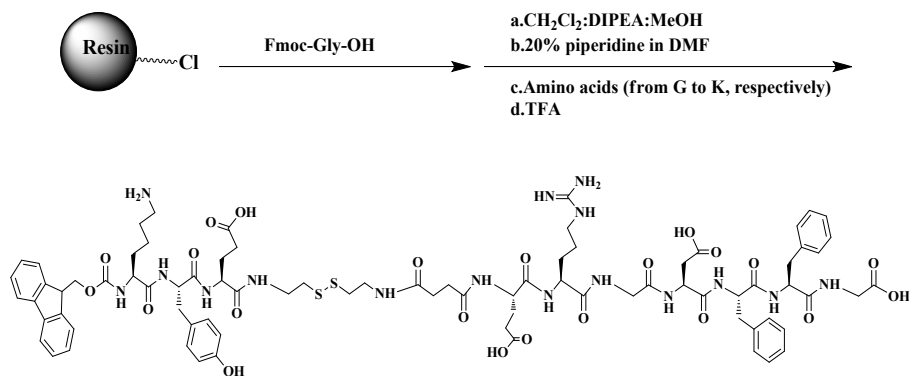
Scheme S-4. Synthetic route for Fmoc-KYE-CS-ERGD-FFG peptide
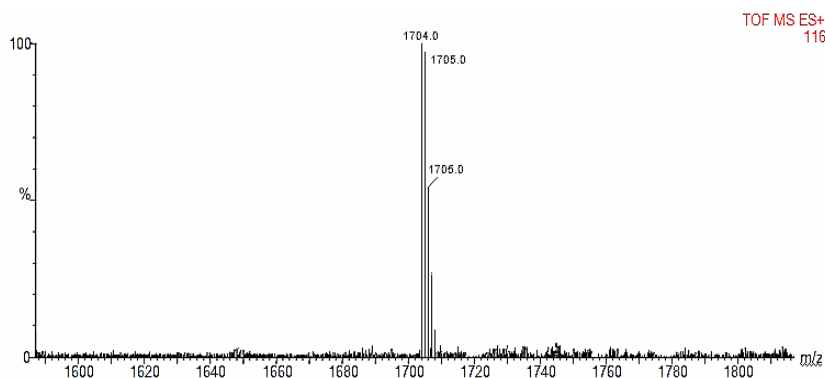
Figure S-13. MS spectrum of Fmoc-KYE-CS-ERGD-FFG peptide
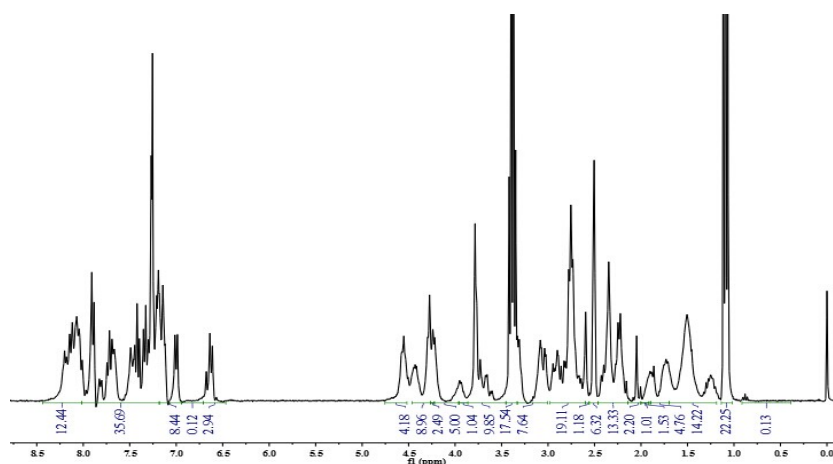
Figure S-14. ¹H NMR spectrum of Fmoc-KYE-CS-ERGD-FFG peptide

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Preparation of Estrone-K(Taxol)YE-CS-ERGD-FFG (Et-Peptide-Taxol, yield of 59.7 %): Fmoc-peptide (0.065g, 0.045 mmol), Taxol–succi-NHS (0.0239g, 0.025 mmol) and DIPEA (35 μL, 0.140 mmol) were dissolved in 2 mL of DMF. The reaction mixture (Fmoc-peptide: Taxol-succi-NHS: DIPEA = 3:2:10) was stirred at room temperature overnight. 0.2 ml of piperidine was added (10% piperidine in DMF) and the solution was stirred at room temperature for 2h. The crude product was poured into 10 ~ 20 times ice-cold ether and was centrifuged for 10 min at 13,000 rpm. The supernatant was dissolved in double-distilled water and lyophilized (yield of 78.4%).

Estrone-succi-NHS (0.041g, 0.087 mmol), NH_2-peptide-Taxol (0.07 g, 0.029 mmol) obtained above and DIPEA (20 μL, 0.232mmol) were dissolved in 2 mL DMF. The resulting reaction mixture (NH_2-peptide-Taxol: Estrone-succi-NHS: DIPEA = 1:3:8) was stirred at room temperature in the dark overnight. The crude product was poured into 10 ~ 20 times ice-cold diethyl-ether and was centrifuged for 10 min at 13,000 rpm. The supernatant was dissolved in double-distilled water and lyophilized. The product was purified by HPLC (Shimadzu, Japan). TOF-MS: m/z 2793.1 [M+Na]. ^{1}H NMR (300 MHz, CDCl$_3$) δ 9.19 (s, 1H), 8.31 (s, 1H), 7.96 (d, J = 12.5 Hz, 7H), 7.80 (t, J = 19.8 Hz, 4H), 7.72 – 7.46 (m, 6H), 7.41 (t, J = 13.0 Hz, 5H), 7.27 – 7.13 (m, 19H), 7.11 – 6.88 (m, 11H), 6.64 (d, J = 8.7 Hz, 5H), 6.28 (s, 1H), 6.07 – 5.51 (m, 2H), 5.44 – 5.23 (m, 3H), 4.90 (d, J = 9.2 Hz, 1H), 4.37 (s, 3H), 4.24 (s, 4H), 3.98 (dd, J = 58.3, 51.1 Hz, 13H), 3.76 (s, 3H), 3.71 (d, J = 31.3 Hz, 8H), 3.57 (d, J = 7.7 Hz, 5H), 3.53 – 3.16 (m, 19H), 2.95 (s, 26H), 2.92 – 2.78 (m, 21H), 2.72 (s, 20H), 2.57 (d, J = 5.3 Hz, 11H), 2.49 (s, 83H), 2.33 (s, 4H), 2.33 – 1.82 (m, 27H), 2.06 – 1.82 (m, 3H), 2.06 – 1.80 (m, 3H), 1.60 (dd, J = 51.3, 30.5 Hz, 44H), 1.22 – 0.93 (m, 23H), 0.81 (s, 1H).
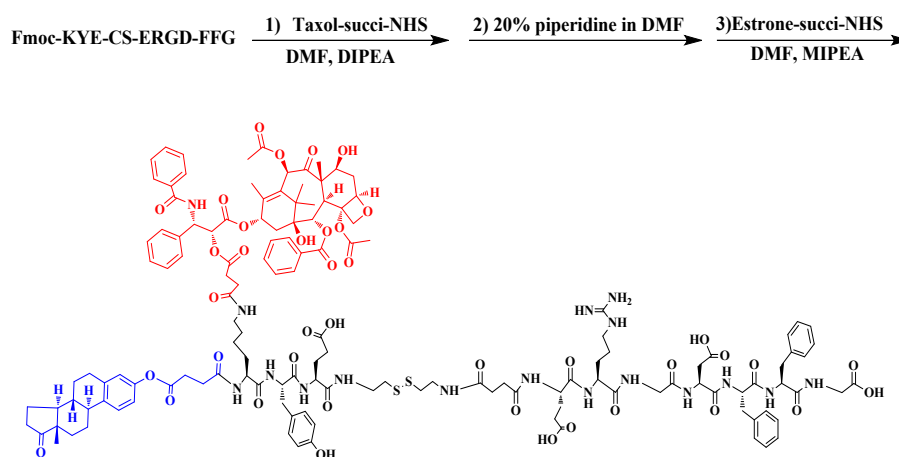
Scheme S-5. Synthetic route for Et-K (Taxol) YE-CS-ERGD-FFG (Et-Peptide-Taxol) compound
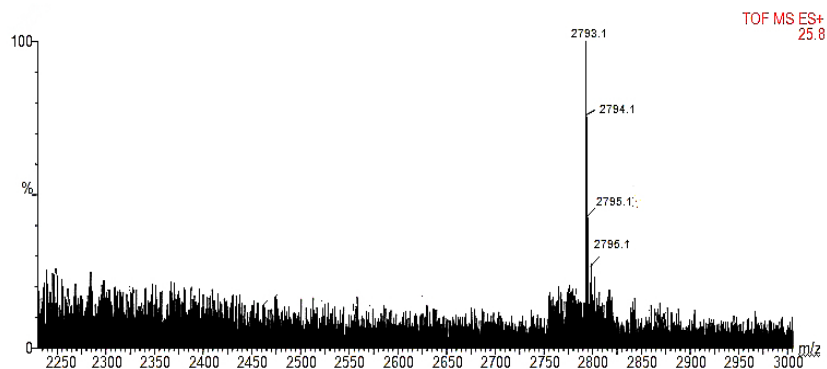
Figure S-15. LC-MS spectrum of Et-K (Taxol) YE-CS-ERGD-FFG (Et-peptide-Taxol) compound
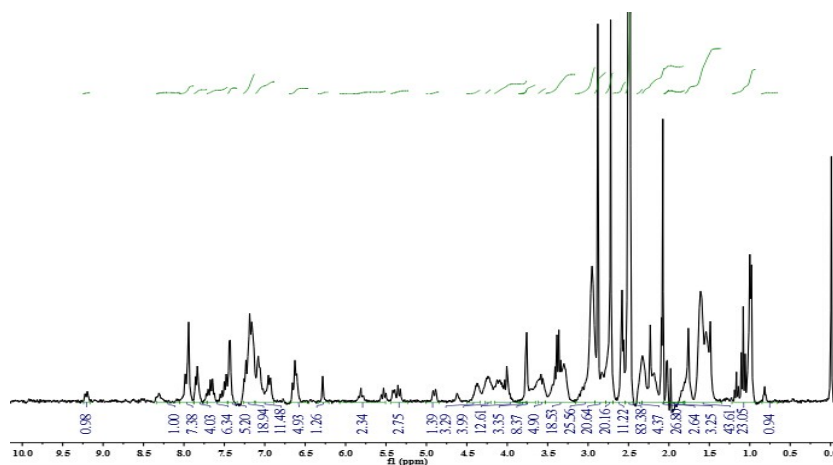

Figure S-16. ^{1}H NMR spectrum of Et-K (Taxol) YE-CS-ERGD-FFG (Et-Peptide-Taxol) compound

Et-KYE-CS-ERGD-FFG (Et-peptide carrier, yield of 43.5%): TOF-MS: m/z 1855.9 [M+Na]. ^{1}H NMR (300 MHz, DMSO) δ 8.62 (t, J = 66.6 Hz, 4H), 7.95 (s, 2H), 7.78 (s, 1H), 7.49 (s, 1H), 7.33 − 7.13 (m, 7H), 7.10 (s, 3H), 6.98 (d, J = 7.7 Hz, 1H), 6.66 (d, J = 7.8 Hz, 2H), 4.39 (s, 3H), 3.42 (s, 5H), 2.91 (d, J = 13.7 Hz, 16H), 2.73 (s, 11H), 2.58 (s, 3H), 2.50 (s, 7H), 2.32 (s, 5H), 2.11 (d, J = 14.3 Hz, 4H), 2.03 (s, 2H), 1.80 (s, 5H), 1.57 (d, J = 20.5 Hz, 20H), 0.99 (d, J = 6.5 Hz, 1H), 0.82 (s, 1H).
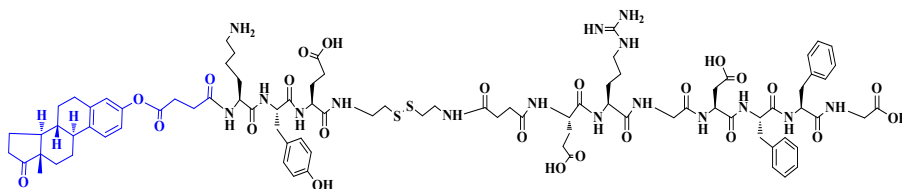
Figure S-17. Structure of Et-KYE-CS-ERGD-FFG (Et-peptide carrier) compound
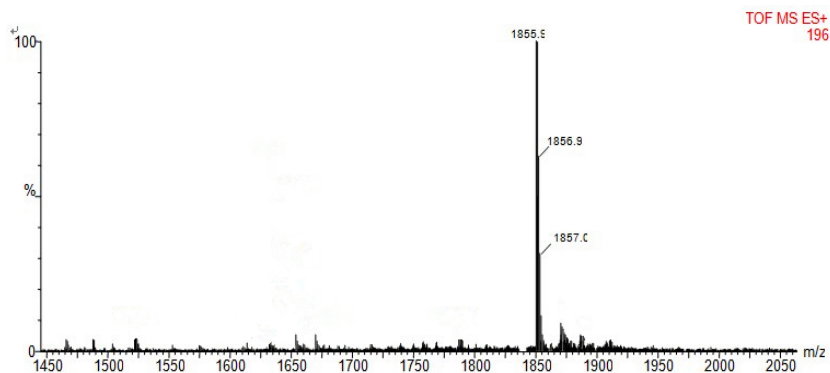
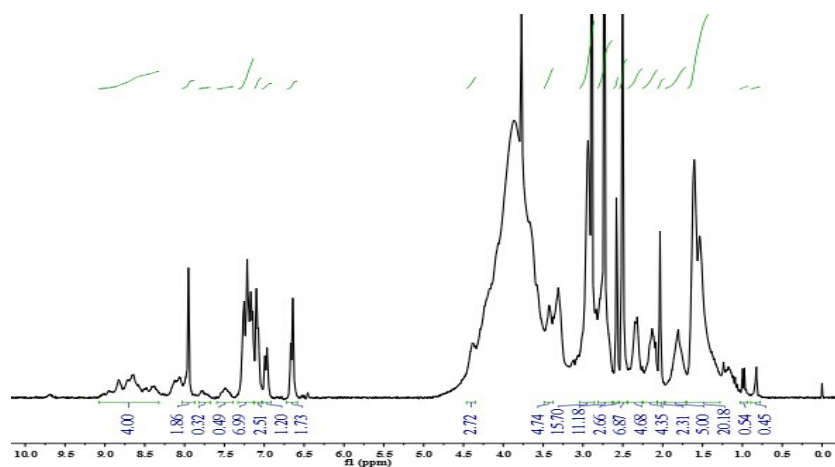**Figure S-18**.LC-MS spectrum of Et-KYE-CS-ERGD-FFG (Et-peptide carrier) compound

Figure S-19. ^{1}H NMR spectrum of Et-KYE-CS-ERGD-FFG (Et-peptide carrier) compound

Nap-KYE-CS-ERGE-FFG (yield of 97.5%): TOF-MS: m/z 1663.7[M$^+$], 1664.7[M+H]. ^{1}H NMR (300 MHz, DMSO) δ 8.84 (s, 1H), 8.29 (d, J = 7.6 Hz, 1H), 8.25 − 7.79 (m, 12H), 7.79 − 7.52 (m, 3H), 7.52 − 7.34 (m, 3H), 7.34 − 6.91 (m, 13H), 6.61 (t, J = 12.2 Hz, 2H), 4.60 − 4.19 (m, 6H), 4.19 − 3.99 (m, 1H), 3.92 − 3.47 (m, 6H), 3.47 − 3.12 (m, 7H), 3.12 − 2.62 (m, 13H), 2.55 (d, J = 27.8 Hz, 3H), 2.24 (dd, J = 32.5, 25.5 Hz, 8H), 2.13 − 2.11 (m, 1H), 2.13 − 1.78 (m, 4H), 2.13 − 1.51 (m, 11H), 1.36 (d, J = 73.1 Hz, 5H), 1.09 (t, J = 7.0 Hz, 6H).
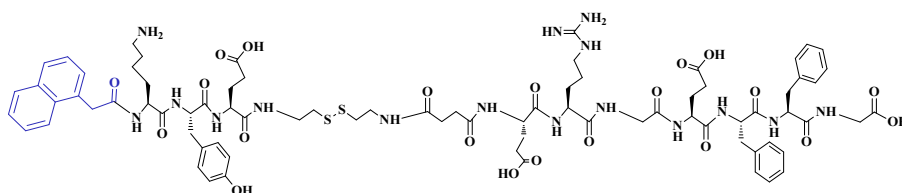

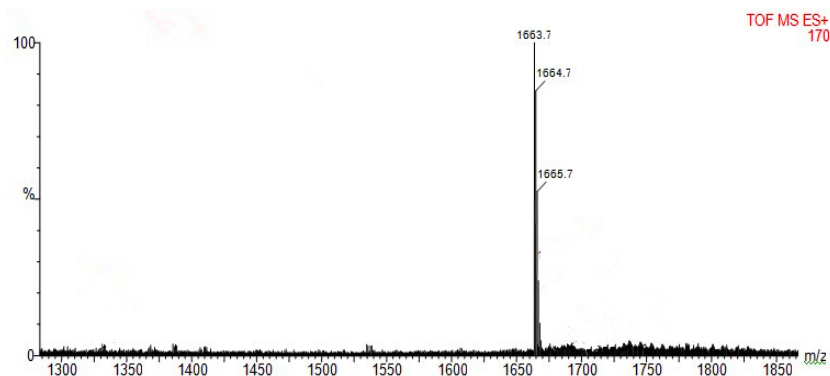**Figure S-20**. Structure of Nap-KYE-CS-ERGE-FFG compound

Figure S-21. MS spectrum of Nap-KYE-CS-ERGE-FFG compound
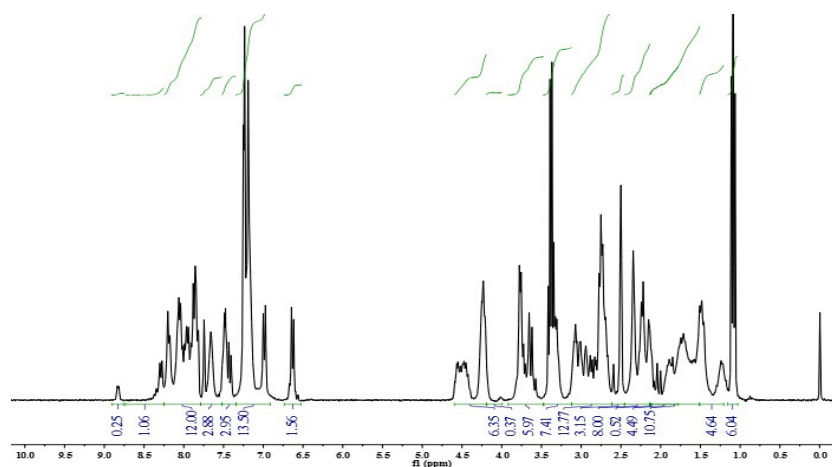

Figure S-22. ^{1}H NMR spectrum of Nap-KYE-CS-ERGE-FFG compound

Nap-K(Taxol)YE-CS-ERGE-FFG (Non-targeting, yield of 89.7%): TOF-MS: m/z 2623.1 [M+Na]. ^{1}H NMR (300 MHz, DMSO) δ 8.84 (s, 1H), 8.29 (d, *J* = 7.6 Hz, 1H), 8.25 − 7.79 (m, 12H), 7.79 − 7.52 (m, 3H), 7.52 − 7.34 (m, 3H), 7.34 − 6.91 (m, 13H), 6.61 (t, *J* = 12.2 Hz, 2H), 4.60 − 4.19 (m, 6H), 4.19 − 3.99 (m, 1H), 3.92 − 3.47 (m, 6H), 3.47 − 3.12 (m, 7H), 3.12 − 2.62 (m, 13H), 2.55 (d, *J* = 27.8 Hz, 3H), 2.24 (dd, *J* = 32.5, 25.5 Hz, 8H), 2.13 − 2.11 (m, 1H), 2.13 − 1.78 (m, 4H), 2.13 − 1.51 (m, 11H), 1.36 (d, *J* = 73.1 Hz, 5H), 1.09 (t, *J* = 7.0 Hz, 6H).
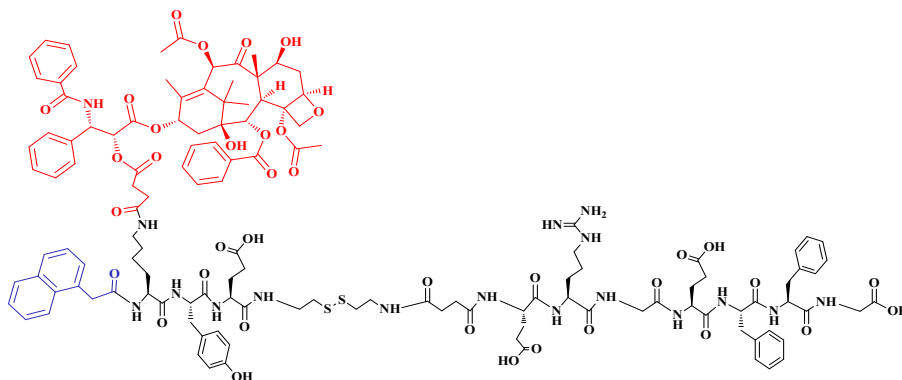

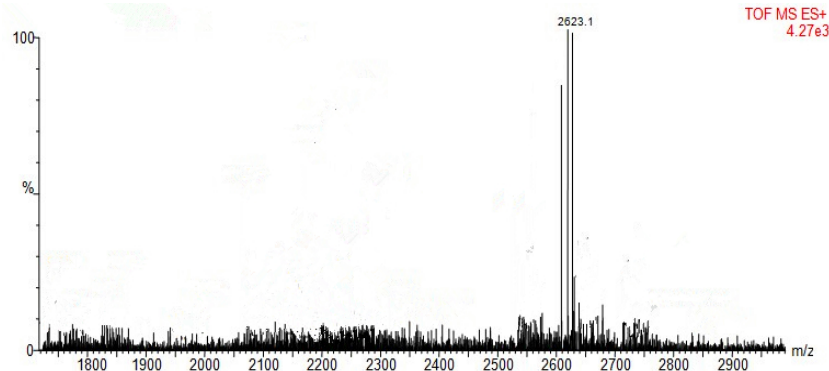**Figure S-23**. Structure of Nap-K (Taxol) YE-CS-ERGE-FFG (Non-targeting) compound

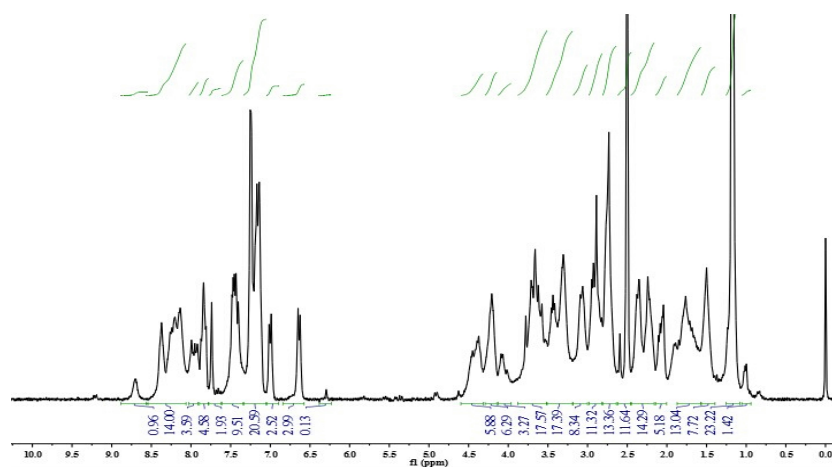**Figure S-24**.LC-MS spectrum of Nap-K (Taxol) YE-CS-ERGE-FFG (Non-targeting) compound

Figure S-25. ^{1}H NMR spectrum of Nap-K (Taxol) YE-CS-ERGE-FFG (Non-targeting) compound

Fmoc-KYE-CS-ERGE-FFG (yield of 78.1%): TOF-MS: m/z 1718.0[M$^+$], 1719.0 [M+H]. ^{1}H NMR (300 MHz, DMSO) δ 8.19 (d, J = 5.8 Hz, 6H), 8.05 (d, J = 6.3 Hz, 12H), 7.89 (d, J = 7.1 Hz, 14H), 7.70 (dd, J = 15.4, 7.1 Hz, 11H), 7.43 (dd, J = 16.6, 8.8 Hz, 9H), 7.32 (t, J = 7.3 Hz, 5H), 7.28 – 7.09 (m, 34H), 7.00 (d, J = 8.2 Hz, 6H), 6.69 – 6.54 (m, 5H), 4.52 (dd, J = 18.7, 10.1 Hz, 8H), 4.25 (d, J = 11.1 Hz, 16H), 3.86 – 3.70 (m, 11H), 3.48 – 3.24 (m, 26H), 3.15 – 2.85 (m, 15H), 2.80 – 2.66 (m, 19H), 2.59 (s, 2H), 2.50 (s, 10H), 2.34 (s, 10H), 2.02 (d, J = 12.6 Hz, 2H), 2.01 – 1.62 (m, 19H), 1.48 (d, J = 15.3 Hz, 18H), 1.27 (d, J = 14.7 Hz, 5H), 1.09 (t, J = 7.0 Hz, 26H).
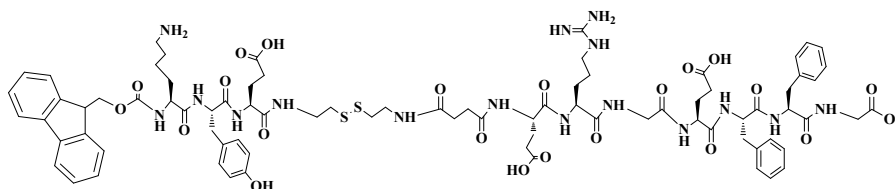
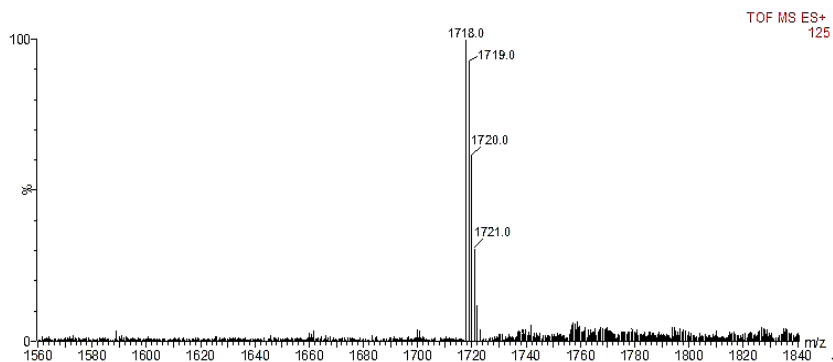

Figure S-26. Structure of Fmoc-KYE-CS-ERGE-FFG compound

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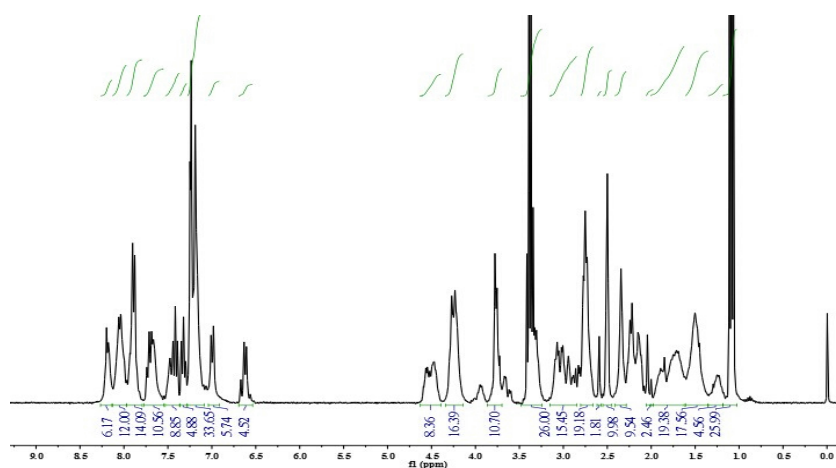**Figure S-27**. MS spectrum of Fmoc-KYE-CS-ERGE-FFG compound

Figure S-28. ^{1}H NMR spectrum of Fmoc-KYE-CS-ERGE-FFG compound

Et-K (Taxol) YE-CS-ERGE-FFG (Single-targeting, yield of 43.5%): TOF-MS: m/z 2807.1 [M+Na]. ^{1}H NMR (300 MHz, DMSO) δ 8.84 (s, 1H), 8.67 (s, 1H), 7.99 (d, J = 23.3 Hz, 4H), 7.61 − 7.40 (m, 1H), 7.14 (ddd, J = 53.7, 27.5, 6.2 Hz, 18H), 6.65 (d, J = 7.9 Hz, 3H), 4.31 (d, J = 43.4 Hz, 2H), 3.70 (d, J = 41.2 Hz, 6H), 3.49 − 3.17 (m, 9H), 2.85 (t, J = 31.3 Hz, 35H), 2.58 (d, J = 3.7 Hz, 3H), 2.50 (s, 15H), 2.31 (s, 6H), 2.15 (s, 4H), 2.00 (d, J = 18.3 Hz, 2H), 1.80 (s, 4H), 1.60 (s, 22H), 1.09 (t, J = 7.0 Hz, 3H), 0.98 (d, J = 6.6 Hz, 2H), 0.82 (s, 1H).
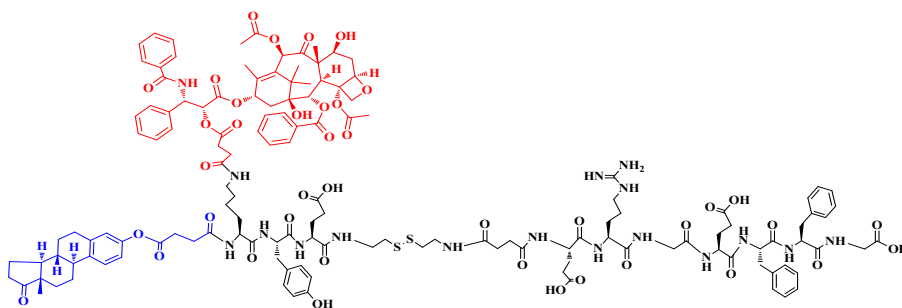

Figure S-29. Structure of Et-K (Taxol) YE-CS-ERGE-FFG ((Single-targeting) compound
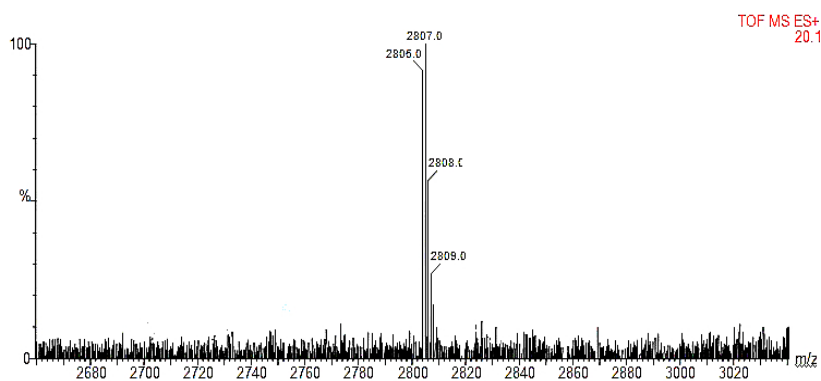
Figure S-30. LC-MS spectrum of Et-K (Taxol) YE-CS-ERGE-FFG ((Single-targeting) compound
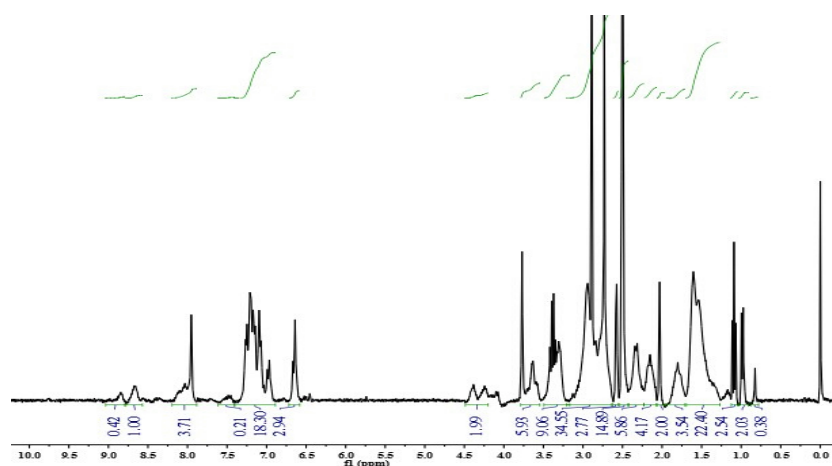

Figure S-31. ^{1}H NMR spectrum of Et-K (Taxol) YE-CS-ERGE-FFG ((Single-targeting) compound

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