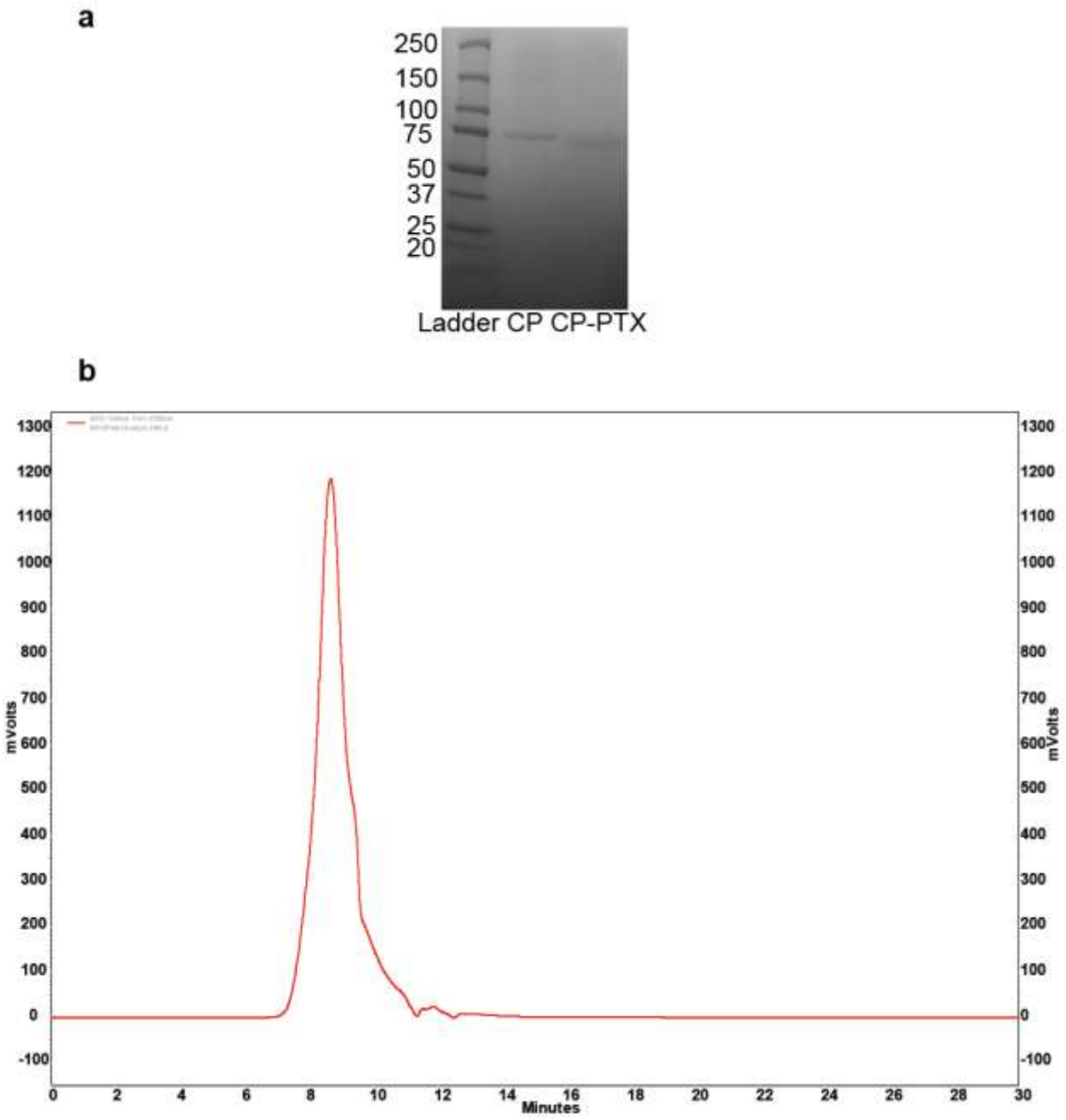
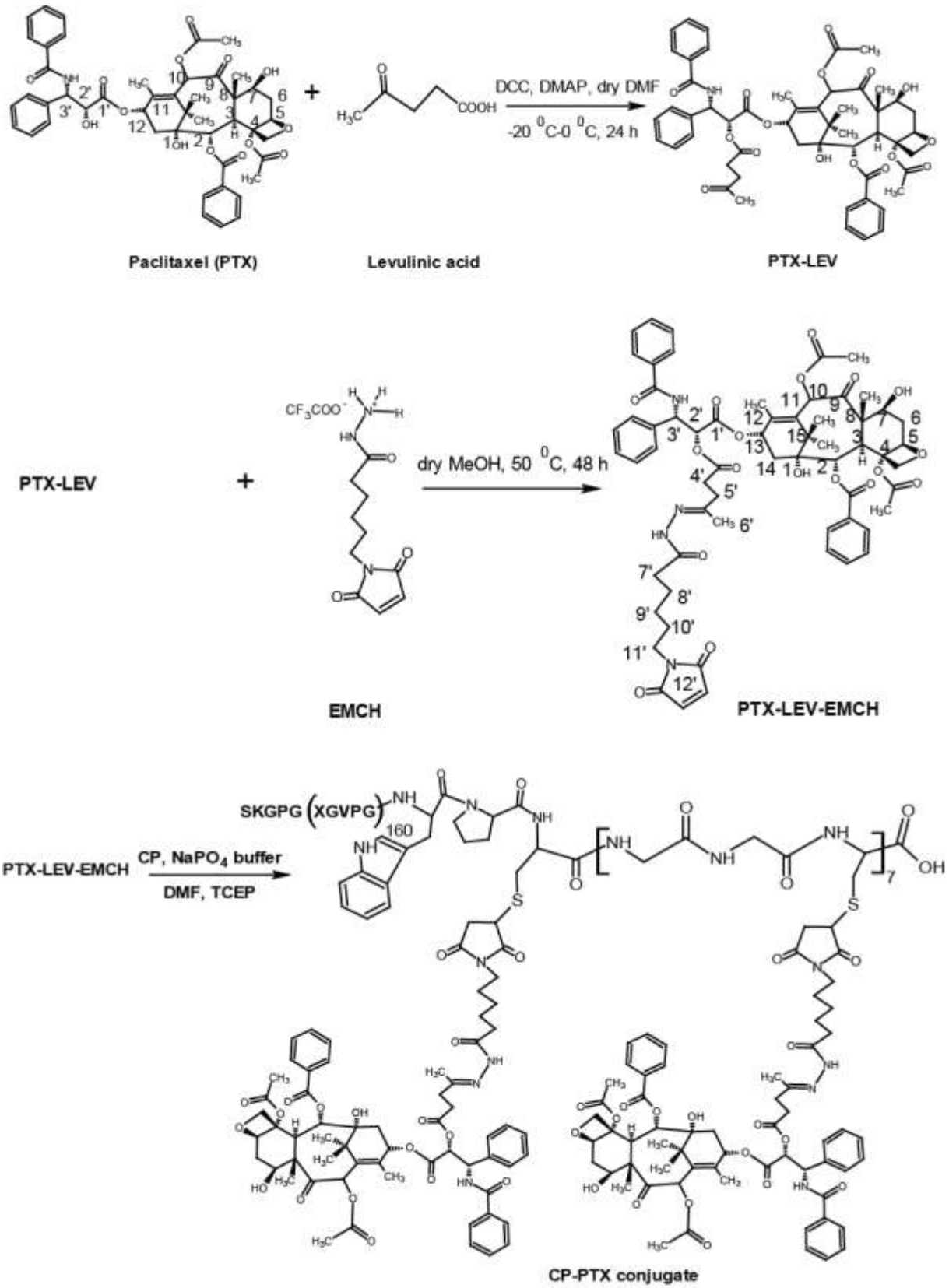
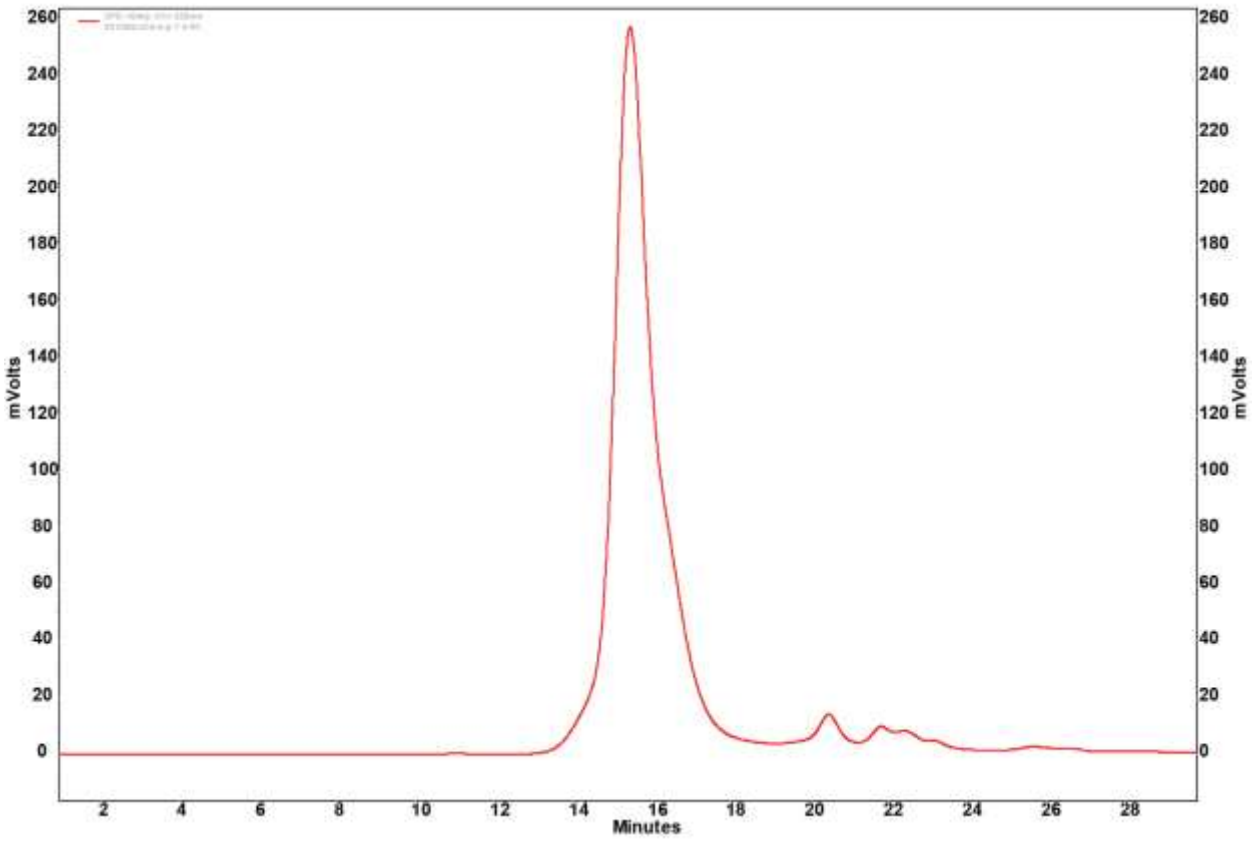


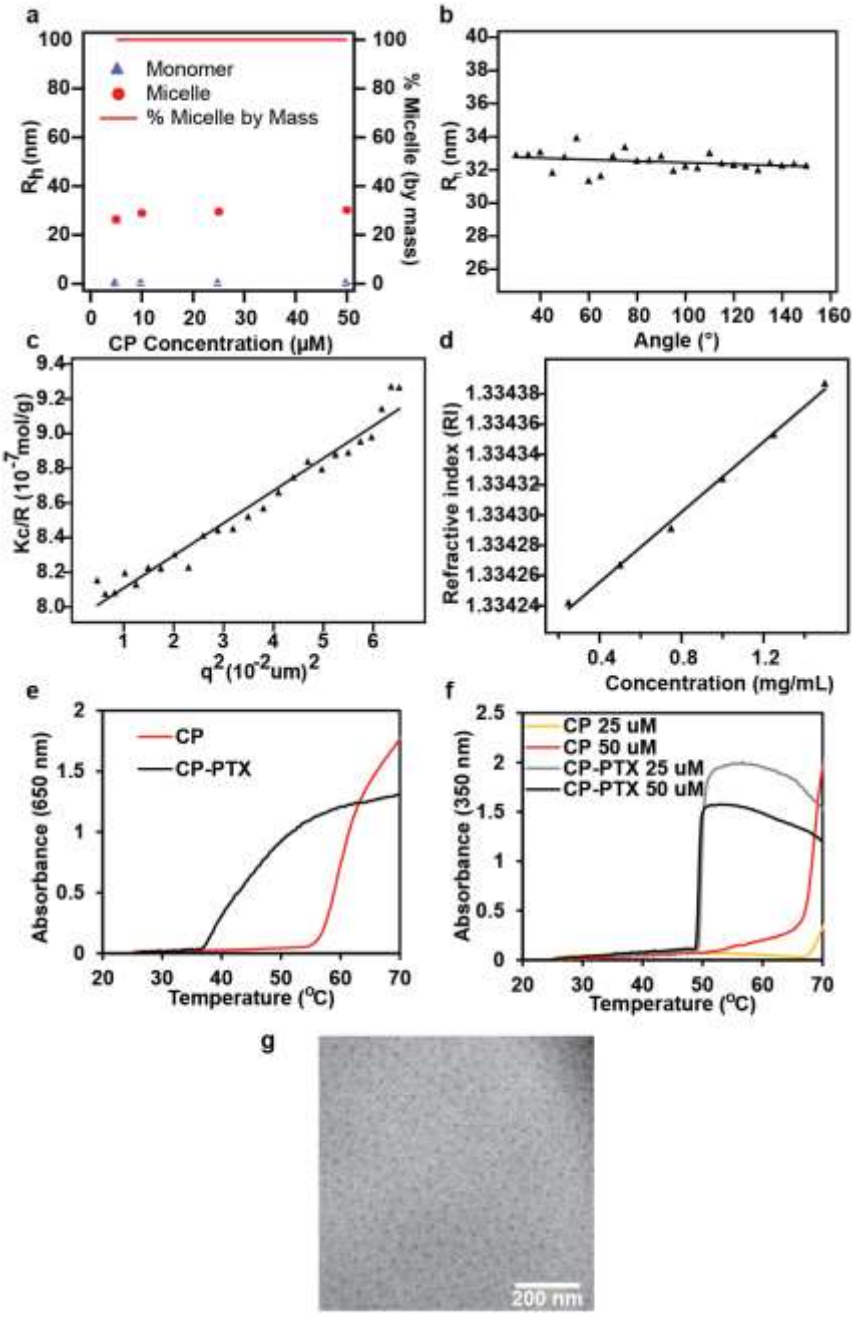
Supplementary Figure 1. **Determination of the purity of CP**. **a**, SDS-PAGE of CP and CP-PTX conjugate, and **b**, HPLC trace of purified CP.



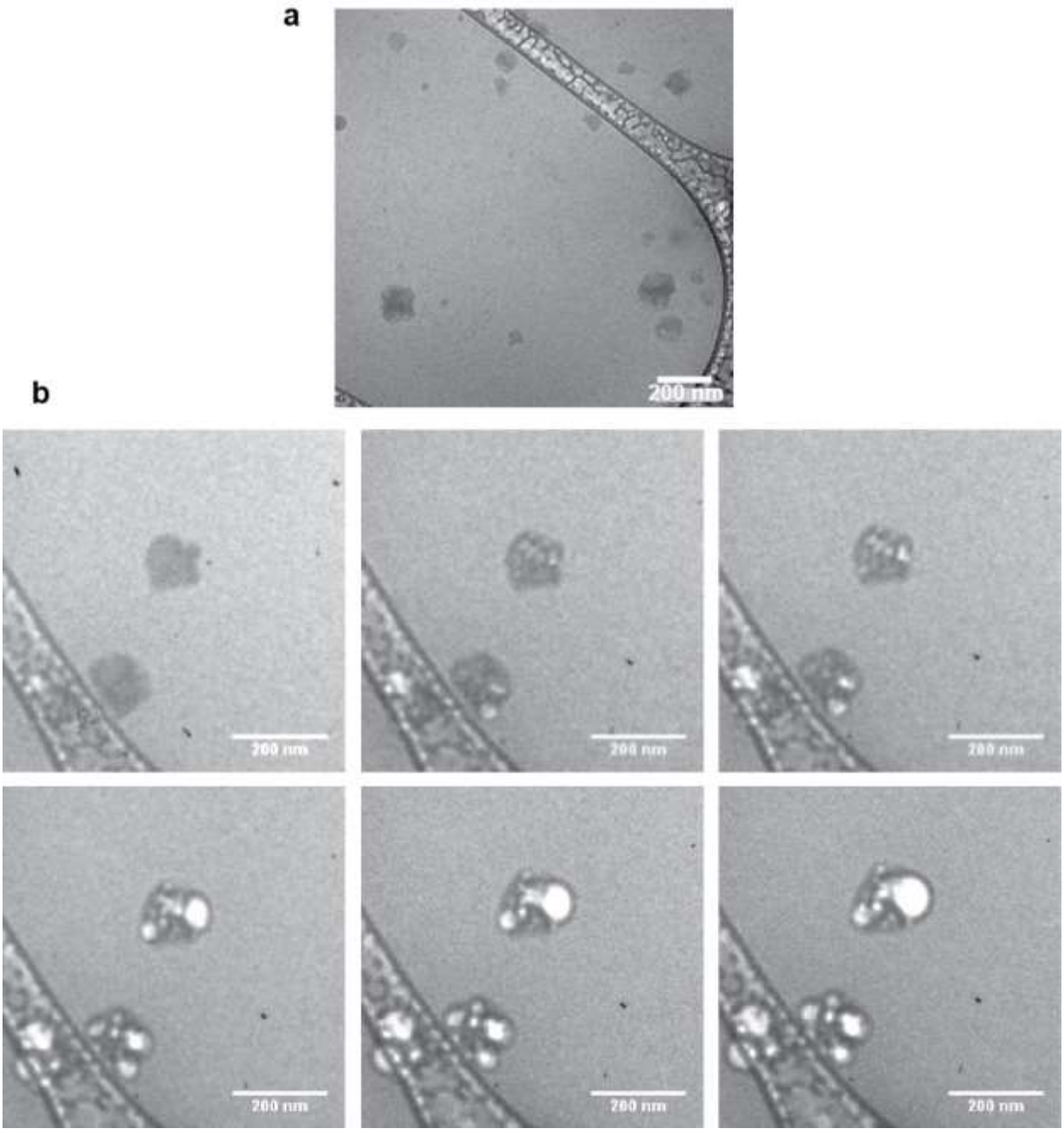
Supplementary Figure 2. Synthesis of CP-PTX conjugate.



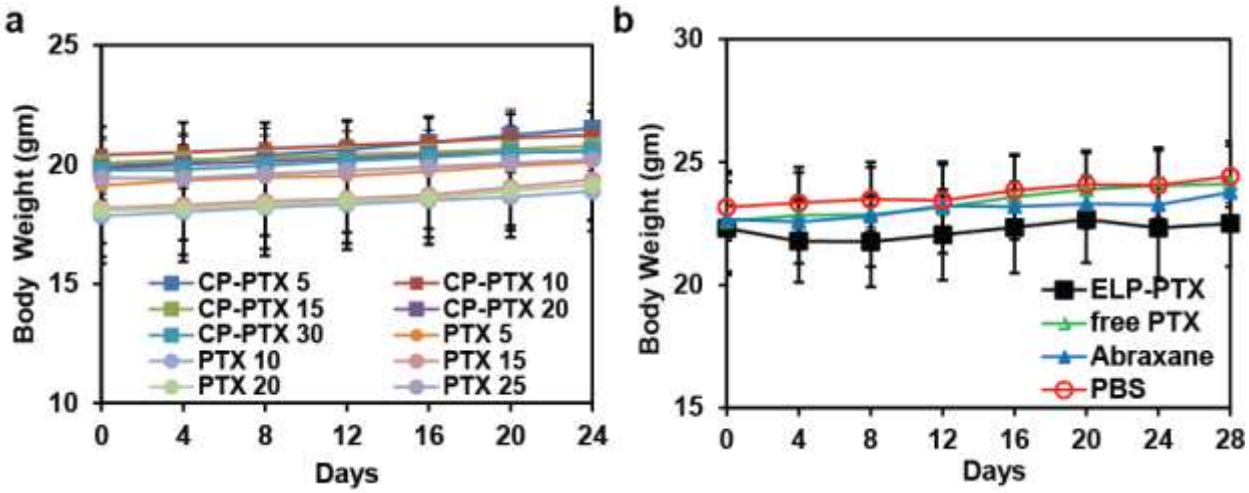
Supplementary Figure 3. **HPLC trace of CP-PTX conjugate.** HPLC was run in a Shodex OHPak SB-804 column (New York, NY) with an isocratic flow of 0.5 mL min^{-1} of PBS: acetonitrile [70:30] was used. The HPLC data was quantified by the integrated area under the peak at an absorbance of 228 nm, corresponding to the absorbance of PTX.



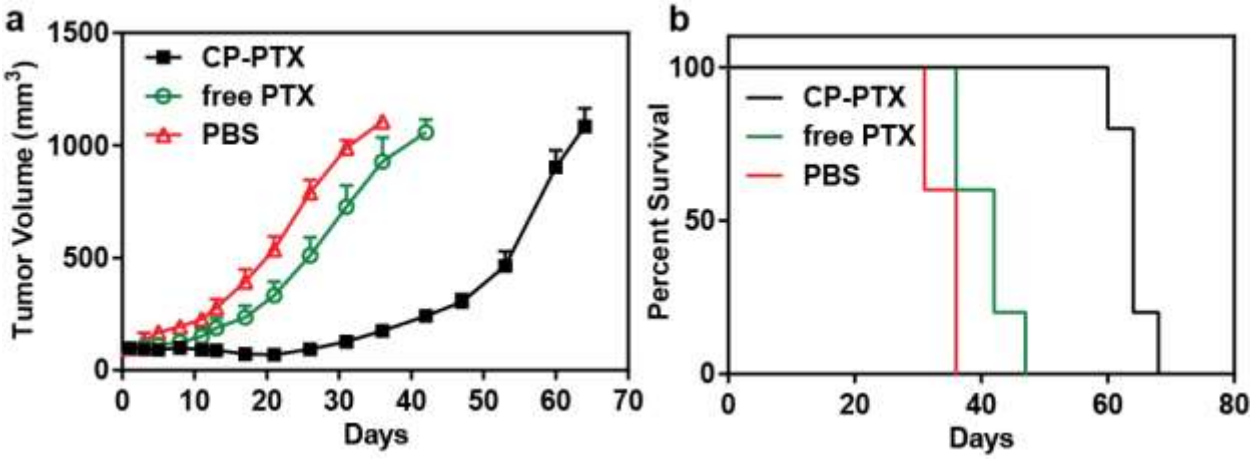
Supplementary Figure 4. **a**, Distribution of hydrodynamic radii for CP and CP–PTX nanoparticles at 5-50 μM in PBS at 37 ^{0}C by DLS. **b**. Angular dependency of hydrodynamic radii for CP–PTX nanoparticles measured by DLS at a concentration of 1.5 mg.mL^{-1} in PBS. **c.** Partial Zimm Plot of Kc/R vs q^2 for CP-PTX conjugate, **d**. Determination of RI of CP-PTX conjugate at different concentration, **e-f**, Determination of transition temperature (T_t) of CP and CP–PTX nanoparticles at 25 and 50 μM in PBS (e) and in mouse serum (f), and **g**. Cryo-TEM picture of CP-PTX conjugate,



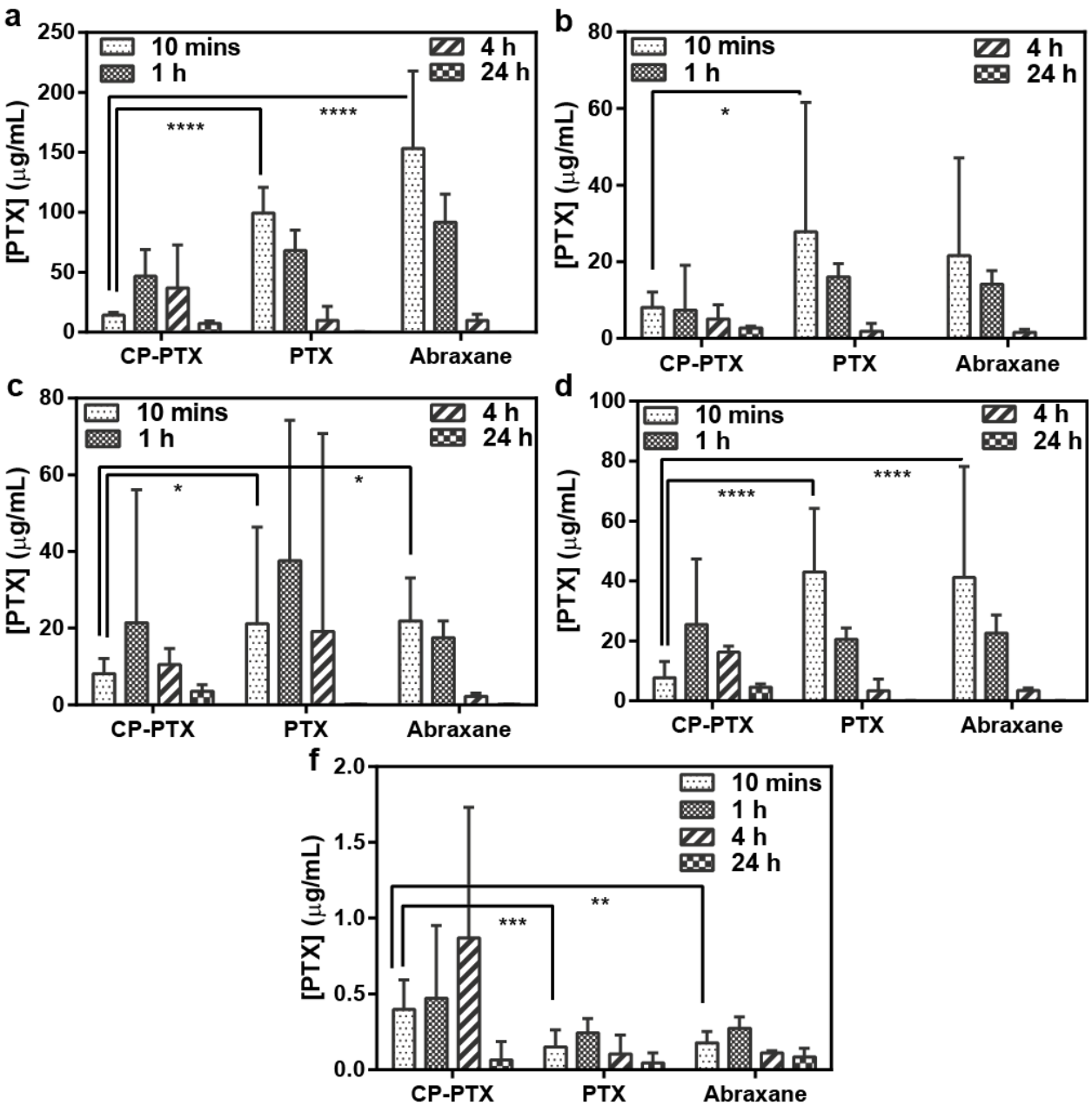
Supplementary Figure 5. **Cryo-TEM picture of Abraxane.** Cryo-TEM picture of Abraxane without (a) or with the exposure of electron beam (b). The damaged particle structure, which was observed as the sample was exposed to the beam for a prolonged period, indicates the presence of organic material (and not ice). Scale bars are 200 nm. In cryo-TEM, as samples are exposed to the electron beam over a prolonged period, bubbling is typically observed as the radiolysis of water causes the formation of free radicals. These free radicals then react with sample molecules to form hydrogen gas.



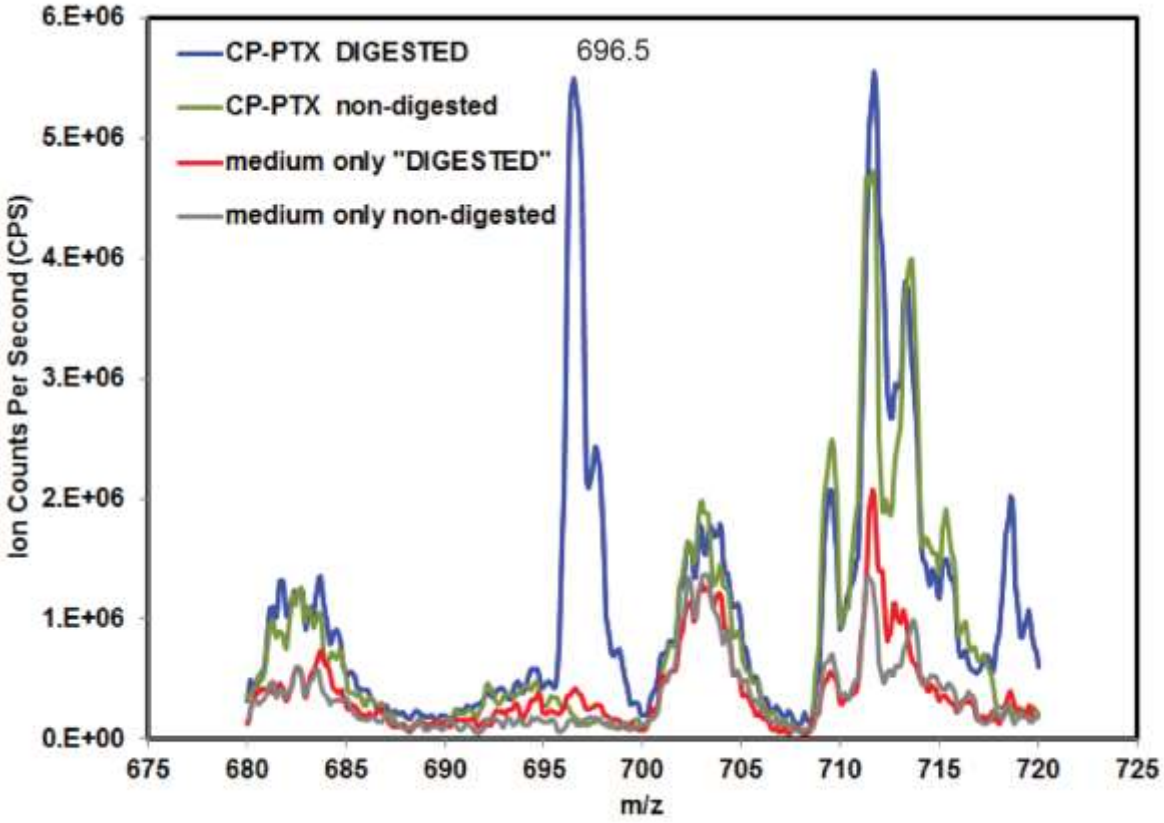
Supplementary Figure 6. **a**. **Dose escalation in mice bearing subcutaneous MDA-MB-231 tumor.** Solutions were systemically administered on day 0. Treatments include CP-PTX, and free PTX at 5-30 mg PTX equiv/kg BW, and 5-25 mg PTX Equiv kg-1 BW respectively. Points represent the mean ± SD (n=5). **b**. Body weight of mice (up to 28 days) bearing orthotopic MDA-MB-231 tumor and were treated with CP-PTX, free PTX, Abraxane and PBS as mentioned in figure 5 a-b.



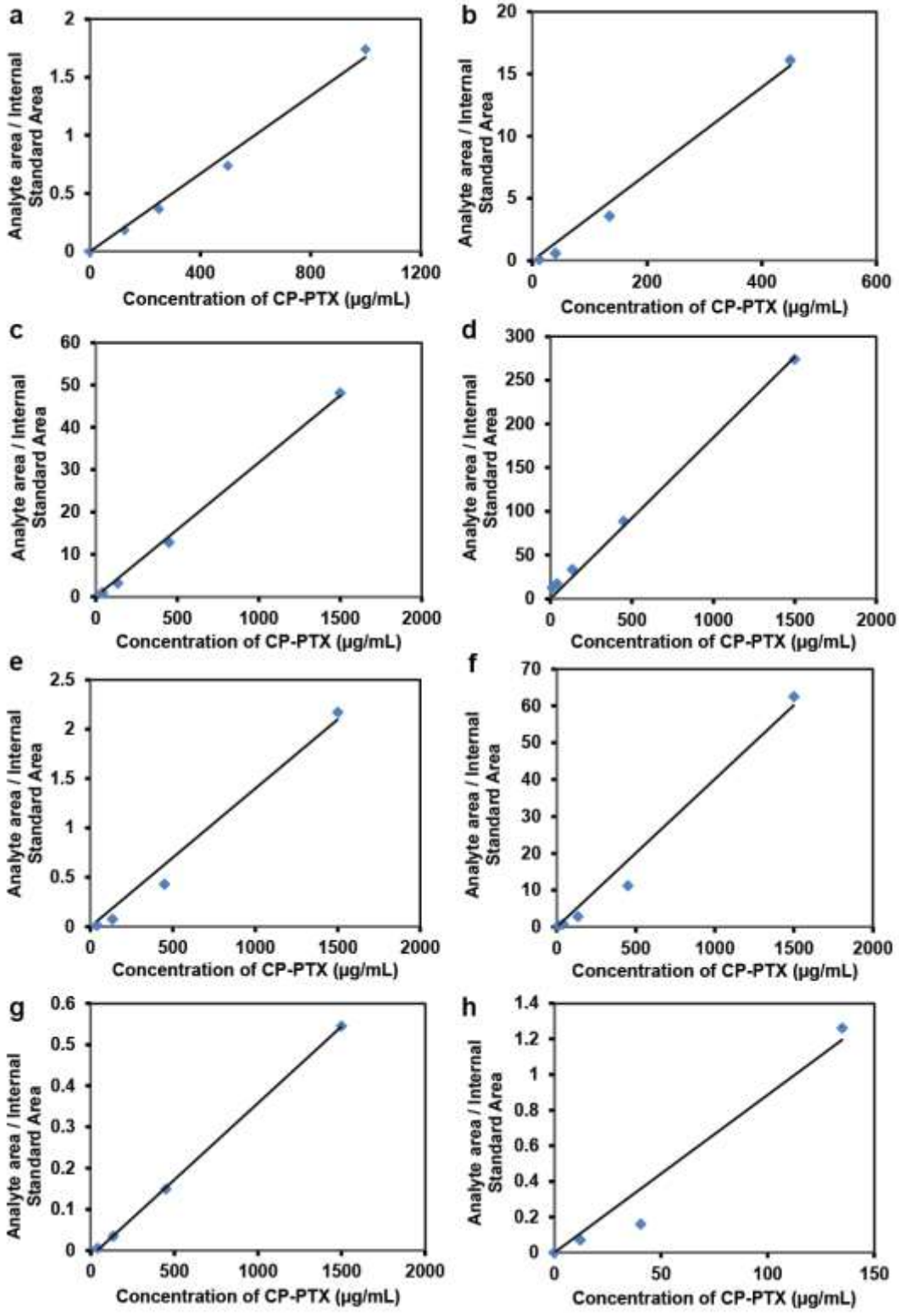
Supplementary Figure 7. Anti-tumor activity of CP–PTX nanoparticles in mice bearing subcutaneous MDA-MB-231 tumor. For **a**, and **b**, tumor cells (MDA-MB-231) were implanted on right flank. When the tumor volume reached ~100 mm^3, mice were treated at the MTD with PBS (*n*=8), free PTX (25 mg kg^{-1} BW, n= 8) and CP–PTX (30 mg PTX Equiv kg^{-1}BW, n= 8). **a**, Tumor volume up to day 64 (mean= ± 95% CI, n= 5). *P*< 0.0001 for CP–PTX versus PTX and PBS (day 31) (Mann–Whitney). **b**, Cumulative survival of mice (Kaplan–Meier).



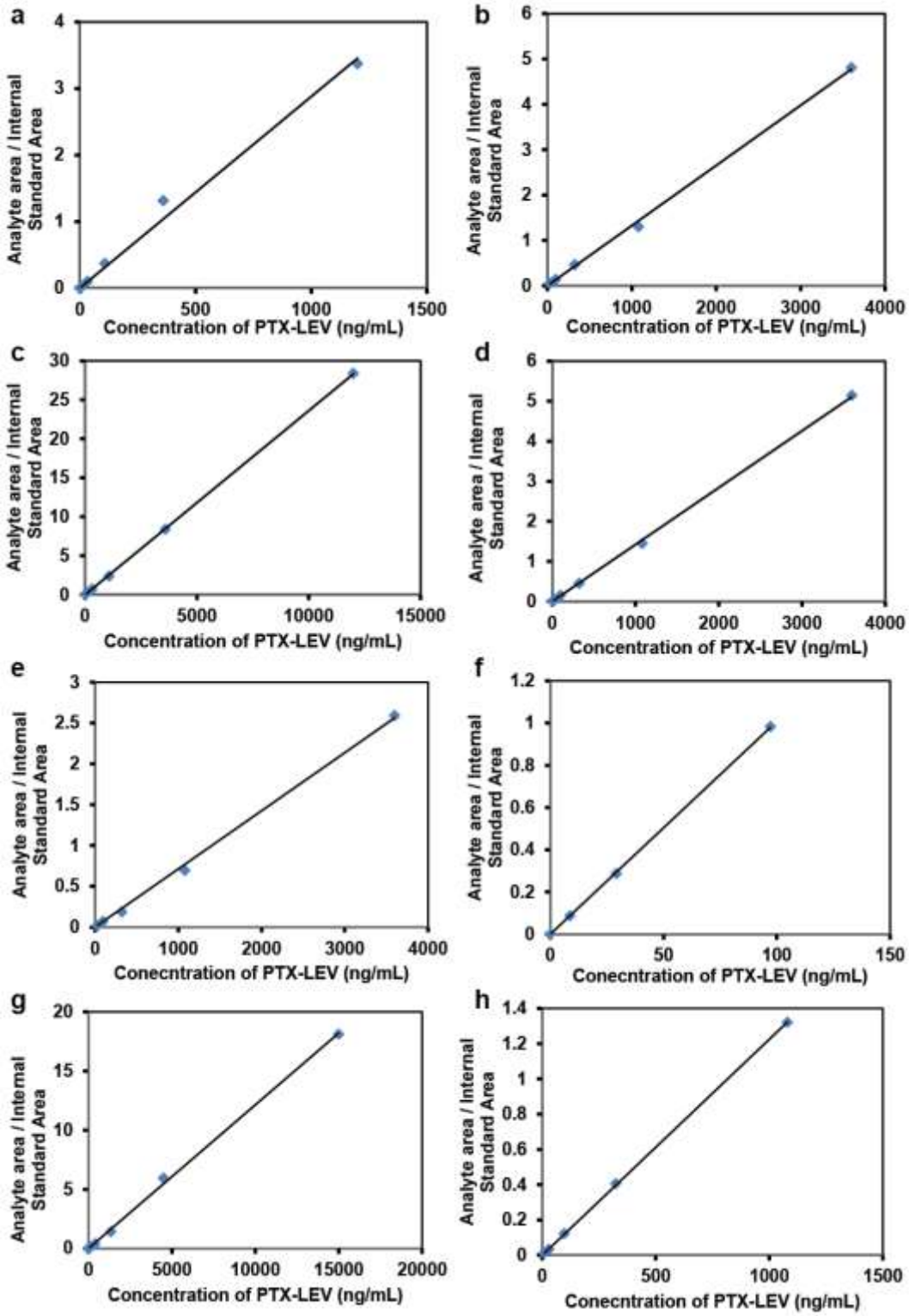
Supplementary Figure 8. Tissue biodistribution. The equivalent PTX concentration in liver (a), heart (b), lung (c), kidney (d), and brain (e) at 10 min, 1 h, 4 h and 24 h post-administration of free PTX and CP-PTX. *, **, **** indicates p< 0.01, 0.001, 0.0001 (analysis of variance, Tukey's test) (mean=±95% CI, n=4).



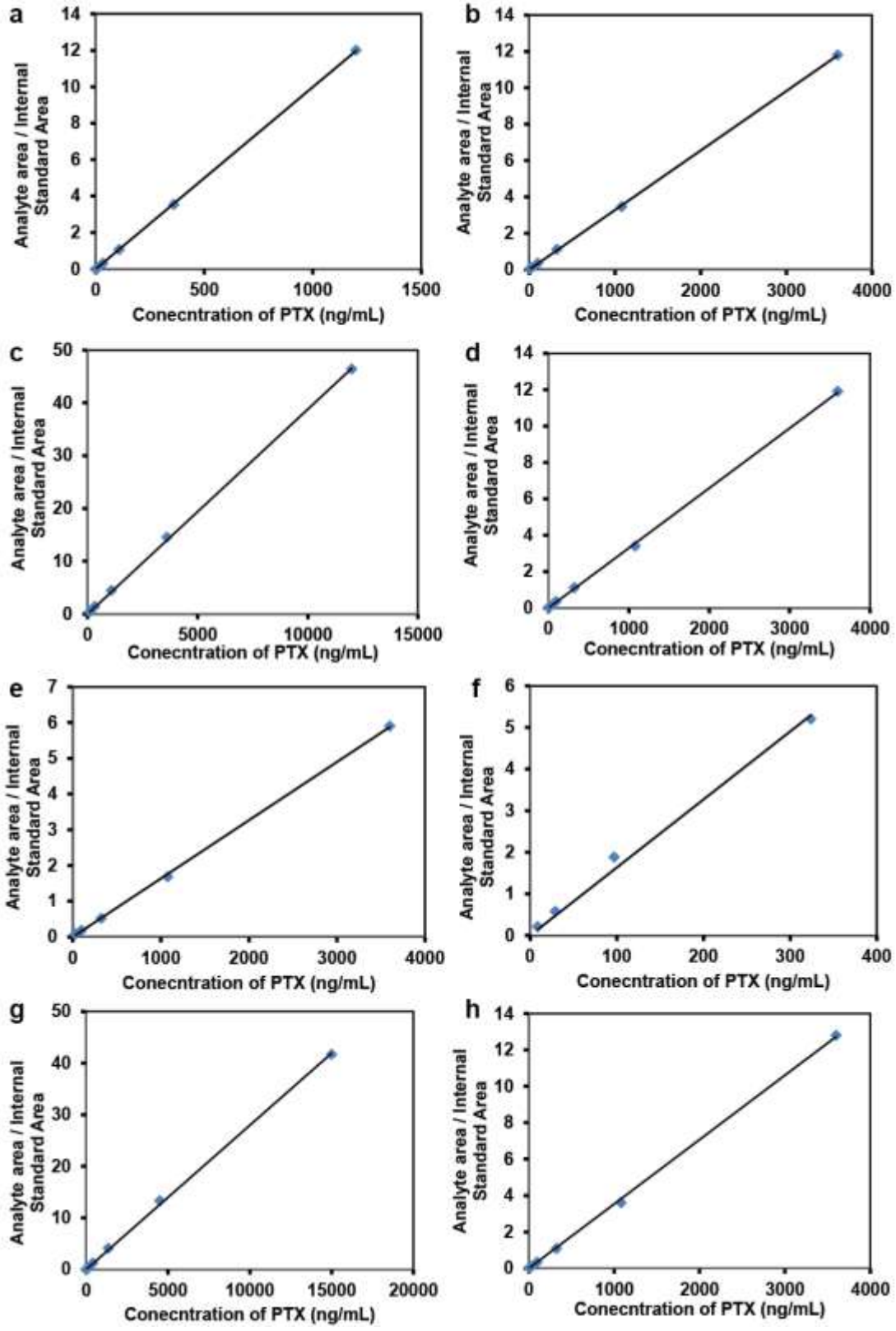
Supplementary Figure 9. Identification of suitable low-molecular-weight fragments for quantification of CP-PTX by LC-MS/MS.



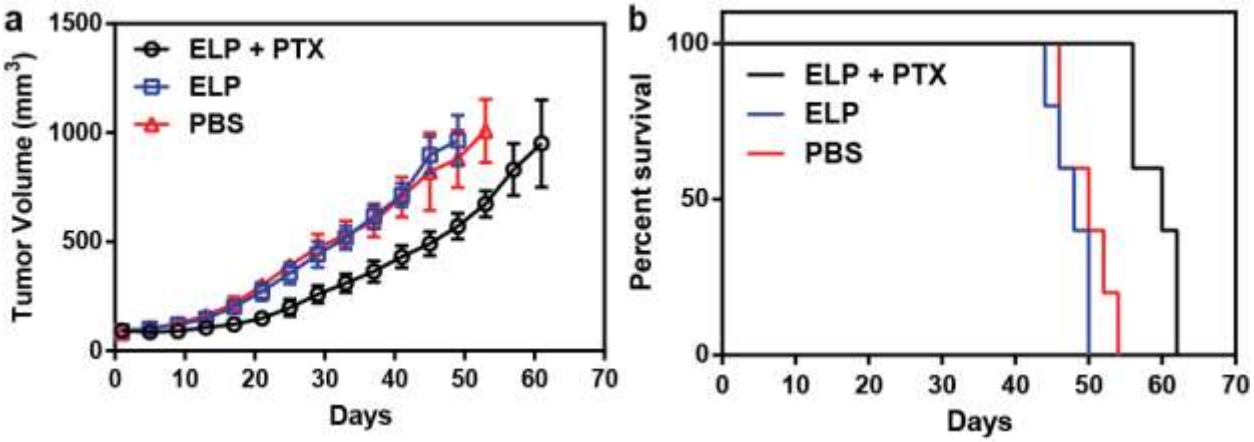
Supplementary Figure 10. Standard curve for the quantification of CP-PTX in in plasma (a), tumor (b), heart (c), lung (d), kidney (e), brain (f), liver (g) and muscle (h) by LC-MS/MS.



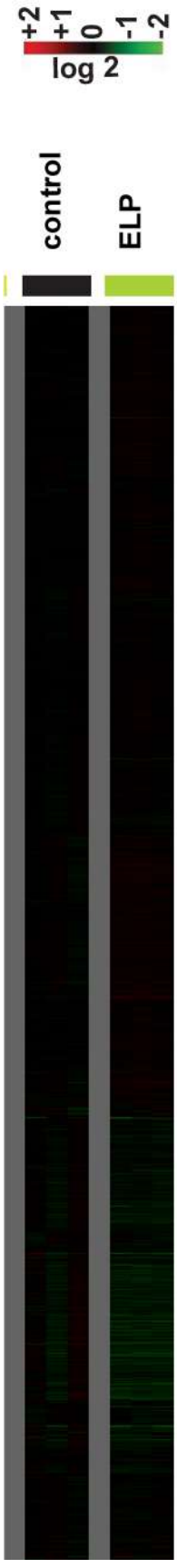
Supplementary Figure 11. Standard curve for the quantification of PTX-LEV in plasma (a), tumor (b), heart (c), lung (d), kidney (e), brain (f), liver (g) and muscle (h) by LC-MS/MS.



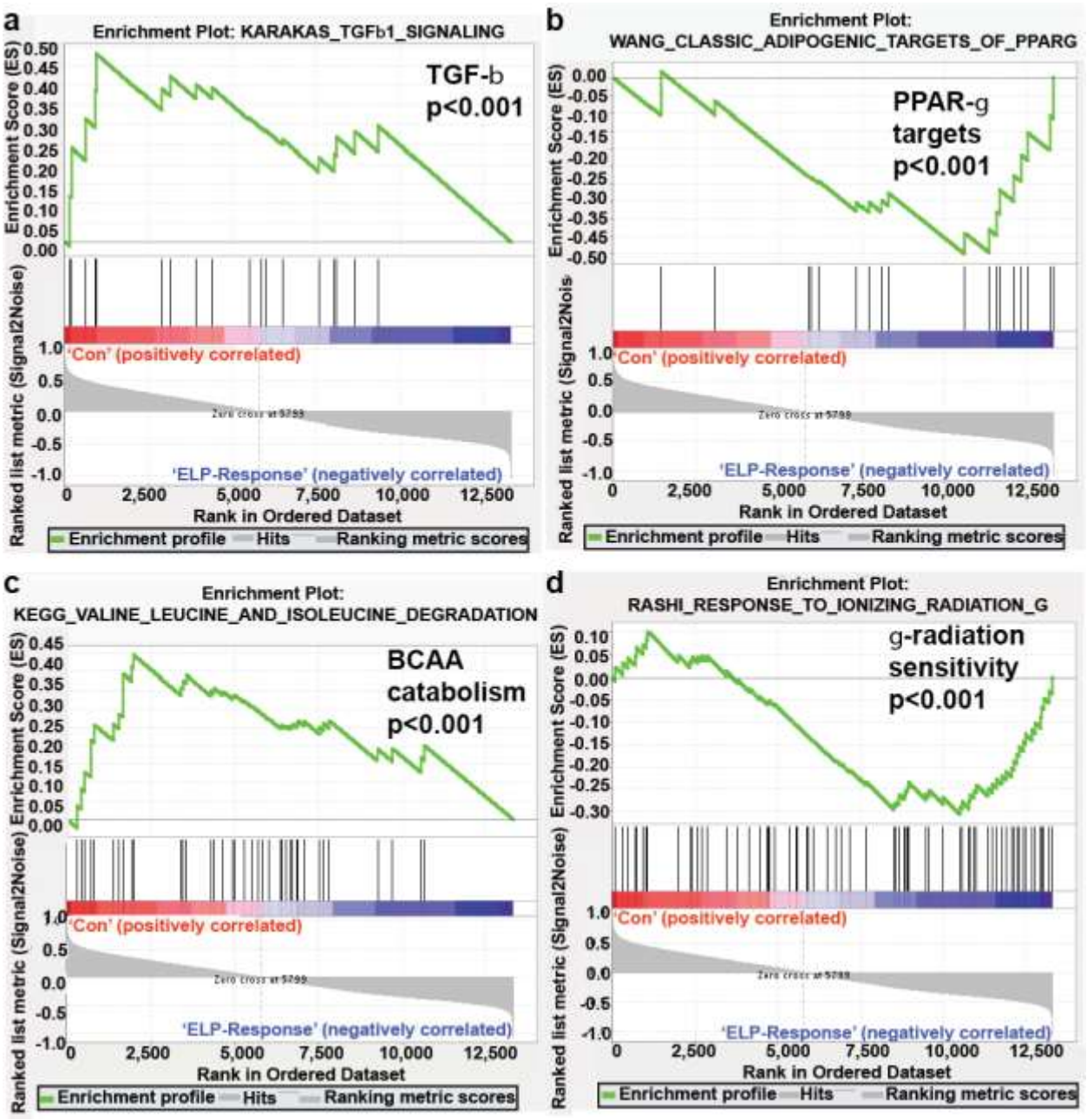
Supplementary Figure 12. Standard curve for the quantification of PTX in plasma (a), tumor (b), heart (c), lung (d), kidney (e), brain (f), liver (g) and muscle (h) by LC-MS/MS.



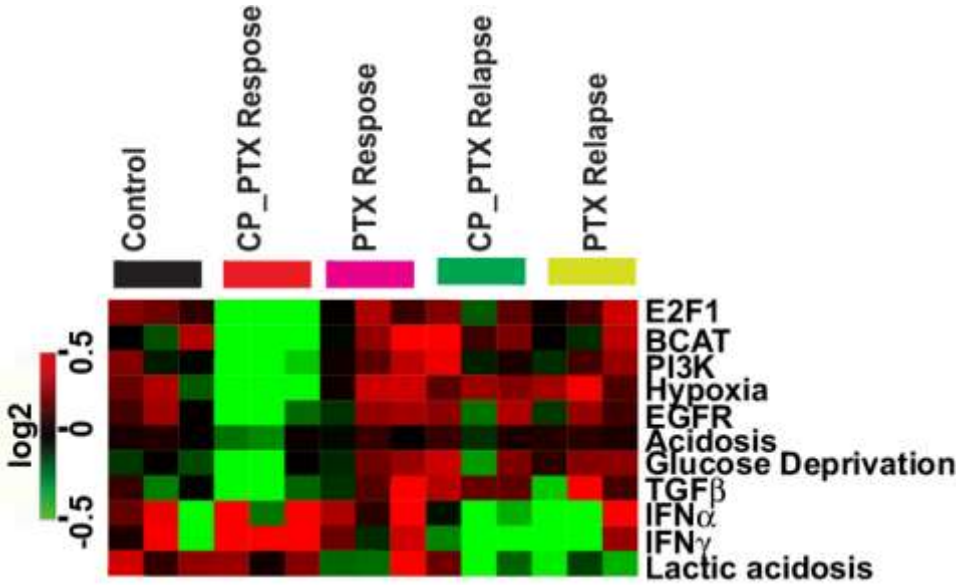
Supplementary Figure 13. Anti-tumor activity of controls. For **a**, and **b**, tumor cells (MDA-MB-231) were implanted on the mammary fat pad on day zero. When the tumor volume reached ~100 mm^3, mice were treated with PBS (*n*=5), ELP (25 mg kg^{-1} BW, n= 5) and ELP+PTX (25 mg PTX equiv.kg^{-1} BW, n= 5). **a**, Tumor volume up to day 62 (mean= ±95% CI, n= 5). *P*< 0.0001 for ELP+PTX versus ELP (day 44) respectively (Tukey test). **b**, Cumulative survival of mice (Kaplan–Meier).



Supplementary Figure 14. **Gene expression analysis of tumors treated with ELP or untreated control**. The global gene expression of xenografts that are responsive to treatment with ELP was determined using microarray analysis using of U133A2 arrays. The transcriptional response of each treatment was derived by zero-transformation. Selected gene clusters that were induced and repressed specifically in the ELP tumors that responded to treatment are highlighted by the color bar.



Supplementary Figure 15. **Gene expression changes of tumors treated with CP-PTX or PTX**. Two gene sets which are depleted (a, c) or enriched (b, d) in the CP-PTX response tumors are shown to indicate the affected biological processes.



Supplementary Figure 16. Oncogenic pathway analysis of the tumors treated with CP-PTX or PTX.

Supplementary Table 1. **Physicochemical properties of the CP-PTX conjugate used in anti-tumor studies.**

CP- polypeptide sequence	SKGPG(XGVPG)160WPC(GGC)7
Guest residues (X)	V:A:G [1:8:7]
Molecular weight of CP (KDa)	62.5
[1]Drugs per CP	2
[2]R_h (nm)	32.5 ±0.6
[2]R_g (nm)	26.6 ± 0.5
[3] Z (chains per nanoparticle)	50
ρ (R_g/R_h)	0.82
dn/dc (mL/g)	1.161E-4
CMC (μM)	1

[1] Drug molecules calculated from MALDI mass spectrometry.
[2] Particle radius determined by DLS at 37 ºC in PBS. Mean ± SD (n=3).
[3] Aggregation number (Z): Number of CP-PTX molecules in a micelle determined by SLS.

Supplementary Table 2. **Physicochemical properties of Abraxane.**

Molecular weight of Abraxane (KD)	73.9
[1]Paclitaxel molecules per albumin	8.7
[2]R_h (nm)	95.5
[2]R_g (nm)	79.3 ± 0.8
[3] Z (albumin proteins/NP)	1757
ρ (R_g/R_h)	0.83
dn/dc (mL/g)	1.156E-4

[1] Number of paclitaxel molecules per albumin calculated by mass: Abraxane is 90% albumin and 10% paclitaxel by mass.
[2] Particle radius determined by DLS at 22 ºC in PBS.
[3] Aggregation number: Number of albumin proteins present in a nanoparticle, determined by SLS.

Supplementary Table 3. IC_{50} of the CP-PTX conjugate and free PTX in MDA-MB-231 cell line.

	CP-PTX	free PTX	Abraxane
IC_{50} (nM) in MDA-MB-231 cells	7.1	2.5	2.7
IC_{50} (nM) in PC3 cells	18.9	5.3	11.9

Supplementary Table 4. Pharmacokinetic parameters of PTX delivered by CP-PTX nanoparticles, Abraxane and free drug.

	Free PTX	Abraxane	CP-PTX		
			[1]PTX	[2]PTX-LEV	[3]CP-PTX
T_{max} (h)	0.2±0.001	0.31±0.0	3.7±1.0	1.3±0.6	0.9±1.0
[4]C_{max} (μgmL^{-1})	21.8±4.2	120.75±94.05	0.6±0.1	7.1±1.4	268±50
$AUC_{(last)}$ ($\mu gmL^{-1}h$)	26.9±8.1	80.47±44.95	15.6±2.2	125.5±16.0	5135±447
$AUC_{(total)}$ ($\mu gmL^{-1}h$)	27.0±8.1	80.81±45.09	17.8±5.2	132±12.8	5282±450
$t_{1/2}$ (h)	1.2±0.3	3.83 ±0.65	13.5±10.0	10.8±2.9	8.4±1.9
[5]CL (Lh^{-1})	0.8±0.2	0.41 ±0.41	1.2±0.3	0.2±0.02	0.004±0.0003
$MRT_{(last)}$ (h)	1.5±0.2	2.43 ±0.71	15.5±1.1	13.1±0.8	13.2±1
$MRT_{(total)}$ (h)	1.5±0.2	2.57±0.76	21.7±10.1	15.9±2.6	14.6±0.9
[5]Vss (L)	1.2±0.3	1.28±1.64	23.7±3.7	2.7±0.6	0.06±0.002

[1] Release of PTX from CP-PTX
[2] PTX-LEV released from CP-PTX
[3] Undegraded CP-PTX in mice treated with CP-PTX
[4]Theoretical C_{max}: 20 mg/kg => 250 ug/mL blood (close to experimentally obtained C_{max} = 265 µg/mL as PTX equiv. in CP-PTX
Dose for PTX-LEV calculated from MW ratio as (20 /853)*951 = 22.3 mg/kg
[5]Dose-dependent parameters (CL and Vss) are "per kg body weight".

Supplementary Table 5. **Biodistribution of PTX (free drug), Abraxane and CP-PTX (values given as PTX equivalents).**

Tissue	Free PTX		Abraxane		CP-PTX[1]	
	10 mins (µg/mg of tissue)	24 hrs (µg/mg of tissue)	10 mins (µg/mg of tissue)	24 hrs (µg/mg of tissue)	10 mins (µg/mg of tissue)	24 hrs (µg/mg of tissue)
Tumor	5.10± 3.53	4.00± 2.11	5.94±1.19	4.57±1.27	6.60±1.72	10.03±2.15
[2]**Muscle**	4.32±2.44	0.033±0.027	7.68±1.57	0.04±0.01	0.77±0.35	0.65±0.59
Heart	27.82±21.25	0.008±0.002	21.67±10.25	0.03±0.00	5.17±1.67	2.77±0.29
Lung	21.17±15.84	0.15±0.03	221.93±4.5	0.18±0.03	8.11±2.49	3.59±1.01
Kidney	43.05±13.31	0.08±0.06	41.17±14.92	0.07±0.01	7.76±3.39	4.61±0.71
Liver	99.52±13.41	0.37±0.14	153.5±25.92	0.26±0.07	14.24±1.48	7.38±1.31
Brain	0.15±0.07	0.04±0.04	0.18±0.03	0.08±0.03	0.39±0.12	0.06±0.07
[3]**Plasma**	13.49±3.97	0±0	120.75±94.04	0.06±0.03	246.58±62.27	88.92±23.20
[4]**Total**	214.62±73.82	4.67±2.4	372.81±152.45	5.29±1.49	289.62±73.49	118.01±29.33

[1]Concentration of CP-PTX given as PTX equivalents.
[2]The indicates the total percentage of the initial dose only from the sample of muscle obtained
[3]PTX concentration is in µg/mL of plasma.
[4]The total recovered dose in the assayed tissues, which does not include drug in other tissues or eliminated from the body.