

**Supporting Information for:**

**Polyphosphoester nanoparticles as biodegradable platform  
for delivery of multiple drugs and siRNA**

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**Table S1.** Size and size distribution (PDI) of the neutral PTX-SOR-PPE nanoparticles before and after freeze-drying. Data are presented as mean  $\pm$  SD (n = 3).

<b>Nanoparticle</b>	<b>Particle size (nm)</b>	<b>PDI</b>
Before freeze-drying	31 $\pm$ 1	0.39 $\pm$ 0.02
Lyophilization without cryoprotectant	216 $\pm$ 86	0.40 $\pm$ 0.07
Lyophilization with 2% mannitol	626 $\pm$ 162	0.68 $\pm$ 0.08
Lyophilization with 0.1% mannitol	46 $\pm$ 7	0.30 $\pm$ 0.00

**Table S2.** The effect of different cryoprotectants (Mannitol (1 mg/mL) and sucrose (10 %)) on the size of siRNA-loaded PPE, PEI, chitosan/Tpp nanoparticles.

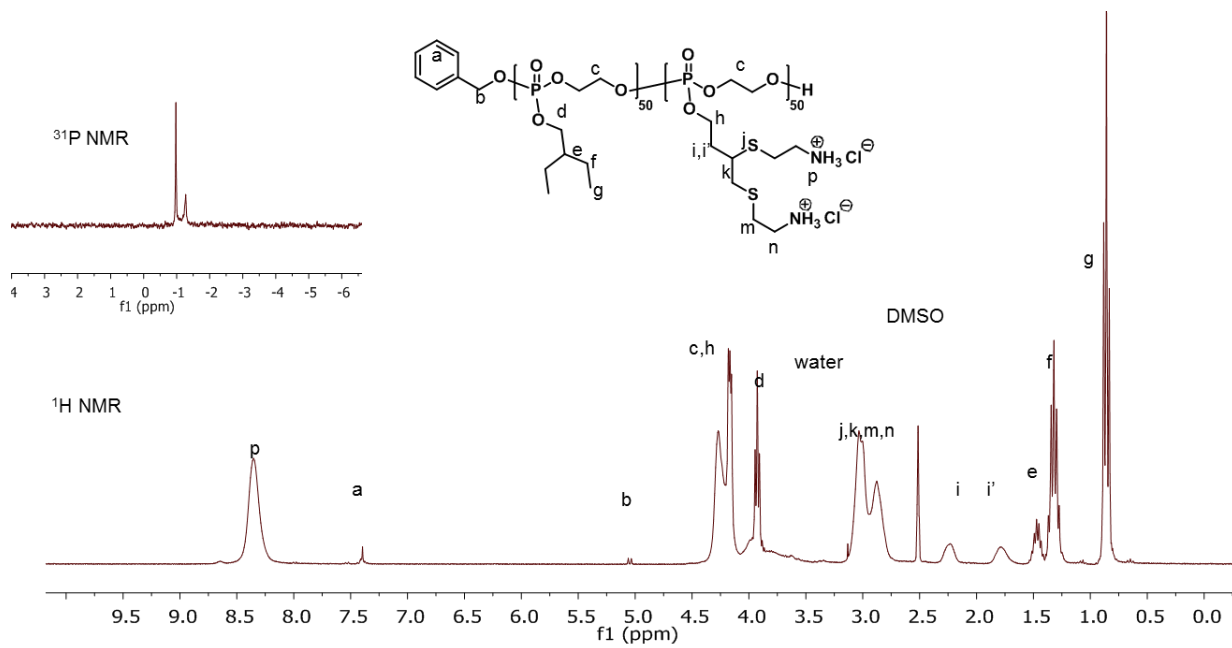
Nanoparticle	No cryoprotectant		Mannitol		Sucrose	
	Before	After	Before	After	Before	After
PPE	137	141	155	125	117	208
PEI	214	247	214	221	214	282
Chitosan/Tpp	244	1112	181	367	206	247

**Table S3.** The effect of different cryoprotectants (Mannitol (1 mg/mL) and sucrose (10 %)) on the PDI of siRNA-loaded PPE, PEI, chitosan/Tpp nanoparticles.

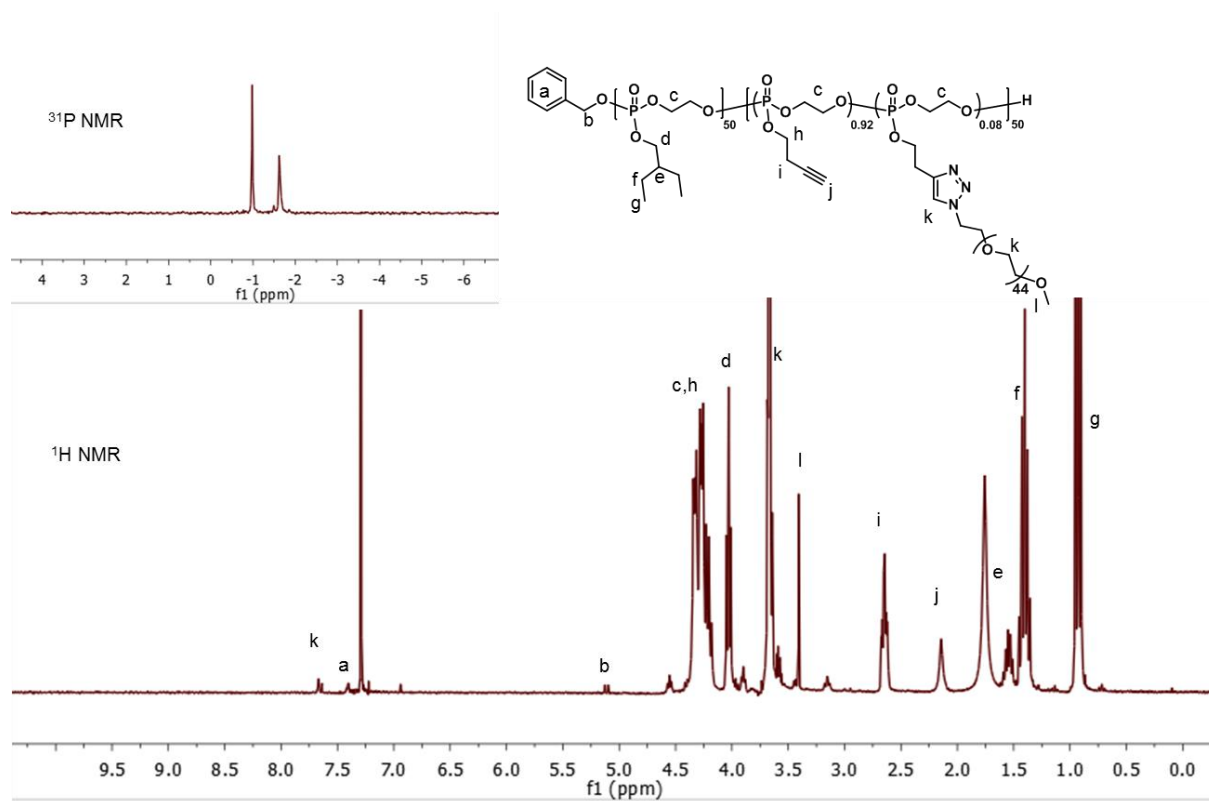
Nanoparticle	No cryoprotectant		Mannitol		Sucrose	
	Before	After	Before	After	Before	After
PPE	0.19	0.29	0.17	0.52	0.19	0.20
PEI	0.48	0.35	0.48	0.31	0.48	0.57
Chitosan/Tpp	0.41	0.23	0.31	0.32	0.27	0.43

**Table S4.** Size, size distribution (PDI) and Zeta-potential measurements of the cationic and neutral PPE nanoparticles complexed with siRNA or loaded with sorafenib (SOR) and (PTX), respectively. The PPE-based cationic and neutral nanoparticles were measured either separately or mixed (with and without further dilution). Data are presented as mean  $\pm$  SD (n = 3).

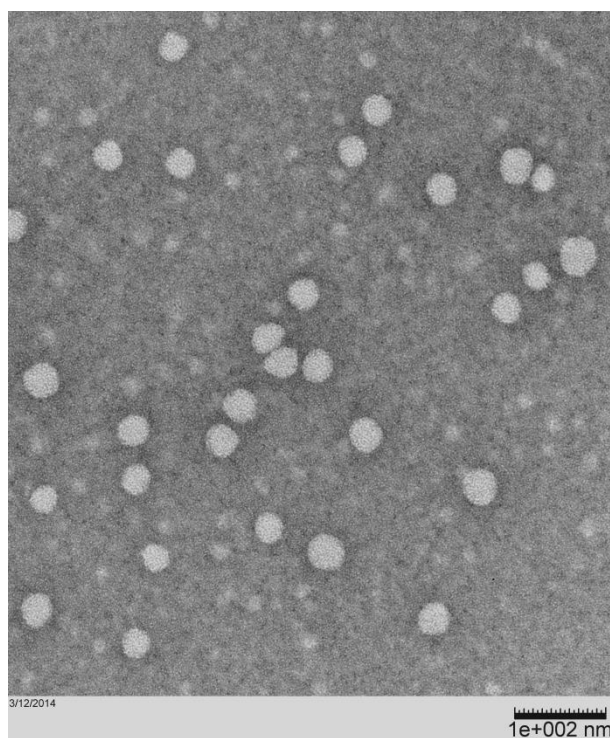
<b>Nanoparticle</b>	<b>Particle size (nm)</b>	<b>PDI</b>	<b>Zeta-potential (mV)</b>
<b>PTX-SOR-PPE nanoparticles Before mixing</b>	45 $\pm$ 1	0.29 $\pm$ 0.003	-34.2 $\pm$ 1.2
<b>siRNA-PPE nanoparticles Before mixing</b>	160 $\pm$ 5	0.40 $\pm$ 0.006	21.6 $\pm$ 0.5
<b>PTX-SOR-PPE/siRNA-PPE nanoparticles (1:1 in water)</b>	83 $\pm$ 1	0.58 $\pm$ 0.010	-2.9 $\pm$ 1.2
<b>PTX-SOR-PPE/siRNA-PPE nanoparticles (1:1 in water and 5 <math>\times</math> dilution)</b>	74 $\pm$ 1	0.40 $\pm$ 0.004	-6.9 $\pm$ 0.4



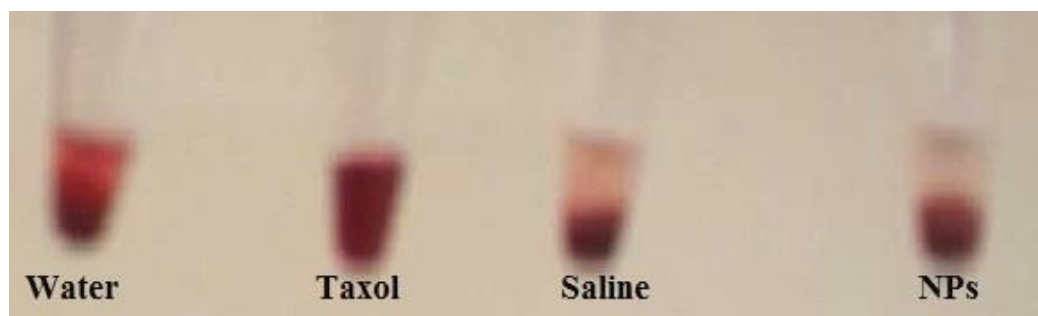
**Figure S1.**  $^1\text{H}$  NMR and  $^{31}\text{P}$  NMR of cationic block copolymer PEBP-*b*-PBYP-C



**Figure S2.**  $^1\text{H}$  NMR and  $^{31}\text{P}$  NMR of PEGylated terpolymer PEBP-*b*-PBYP-*g*-PEG



**Figure S3.** Transmission electron microscopy image of the paclitaxel-loaded nanoparticles.



**Figure S4.** The effect of PTX-SOR-PPE nanoparticles and Taxol<sup>®</sup> solutions on freshly prepared suspension of red blood cells after incubation for 60 min at 37 °C in a shaking water bath at 300 rpm. The PPE nanoparticles tested concentrations are 0.5 mg/mL for paclitaxel and 0.5 mg/mL for sorafenib. Taxol<sup>®</sup> was used as the market mimicking formulation according to the manufacturer instructions (6 mg/mL paclitaxel).



**Figure S5.** The effect of Taxol<sup>®</sup> solution on freshly prepared suspension of red blood cells after incubation for 60 min at 37 °C in a shaking water bath at 300 rpm. Taxol<sup>®</sup> was used as the market mimicking formulation according to the manufacturer instructions, but with slight modifications to contain 0.5 mg/mL paclitaxel and 0.5 mg/mL sorafenib.