Nanoparticles of poly([N-(2-hydroxypropyl)]methacrylamide)-b-poly[2-(diisopropylamino)ethyl methacrylate] diblock copolymer for pH-triggered release of paclitaxel


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Characterization of PHPMA

Figure S1A. SEC traces of the PHPMA macroCTA chain transfer agent utilized as macromolecular chain transfer agent for block copolymer synthesis via RAFT.

Figure S1B. $^1$H NMR spectra of the PHPMA in D$_2$O.
Figure S2A. SEC traces of the PHPMA<sub>25</sub>-b-PDPA<sub>106</sub> block copolymer synthesized via RAFT.

Figure S2B. <sup>1</sup>H NMR spectra of the PHPMA<sub>25</sub>-b-PDPA<sub>106</sub> in D2O/DCI (pH 2).
**Fig. S3.** Static light scattering measurements ($Kc/R\theta$ vs. $q^2$) for PHPMA$_{25}$-b-PDPA$_{106}$ block copolymer NPs in PBS at 25 °C ($R_g \sim 24$ nm and $M_w \sim 1.2 \times 10^6$ g/mol).

**Fig. S4A.** Cell viability of HeLa cell line after 24 h incubation with different concentrations of drug-free PHPMA$_{25}$-b-PDPA$_{106}$ block copolymer NPs.

**Fig. S4B.** Cell viability of HeLa cell line after 48 h incubation with different concentrations of drug-free PHPMA$_{25}$-b-PDPA$_{106}$ block copolymer NPs.
**Fig. S5.** Volume-weighted size distribution for the PHPMA$_{25}$-b-PDPA$_{106}$ NPs at pH 7.4 (black open circles) for the nanoparticles at pH 5.0 (red open squares) and the single block copolymer at pH 5.0 (blue dashed lines) and angle 173° at concentration of 1 mg·mL$^{-1}$ diluted in PBS at 37 °C.

**Fig. S6.** Drug release profiles from paclitaxel-loaded PHPMA$_{25}$-b-PDPA$_{106}$ block copolymer NPs at pH of simulated transport in blood, at pH 6.5 (end stage of protonated process) and simulating the acidic environment in endosomal and lysosomal compartments at 37 °C.
Supporting Table ST1. Synthetic parameters and molecular weight data of polymers prepared via RAFT polymerization.

<table>
<thead>
<tr>
<th>Sample</th>
<th>[M][/CTA][/I]</th>
<th>Time (h)</th>
<th>Conv. (%)</th>
<th>$M_{\text{calc}}$b</th>
<th>$M_{\text{SEC}}$c</th>
<th>$D$c</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHPMA25</td>
<td>120/2/1e</td>
<td>10</td>
<td>36</td>
<td>3 200</td>
<td>3 600†</td>
<td>1.07†</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(2 900)</td>
<td>(1.22)</td>
<td></td>
</tr>
<tr>
<td>PHPMA25-PDPA106</td>
<td>300/3/1f</td>
<td>15</td>
<td>94</td>
<td>23 500</td>
<td>26 200</td>
<td>1.29</td>
</tr>
</tbody>
</table>

- Determined by $^1$H NMR in D$_2$O.
- Theoretical $M_n = [M][/CTA]_0 \times \text{conv.} \times \text{MW}_{\text{mon.}} + \text{MW}_{\text{CTA}}$
- Determined by SEC in THF/MeOH 80/20% using PMMA as standard
- Determined by SEC in acetate buffer pH 6.5 using light scattering and RI detectors
- Conditions: DMAc, [M] = 1.2 M, 70 °C
- Conditions: 1,4-dioxane/MeOH 60/40 vol.% [M] = 3 M, 70 °C