Supporting Information

for

Phosphatase-triggered cell-selective release of a Pt(IV)-backboned prodrug-like polymer for improved therapeutic index

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Fig. S1. $^1$H NMR spectrum of DAEP in CDCl$_3$. 

Supporting Figures and Tables
Fig. S2. $^1$H NMR spectrum of DSP in DMSO-$d_6$. 
Fig. S3. $^1$H NMR spectrum of Pt-NHS in DMSO-$d_6$. 
Fig. S4. $^{13}$C NMR spectrum of Pt-NHS in DMSO-$d_6$. 
Fig. S5. HR-ESI-MS spectrum of Pt-NHS.
Fig. S6. GPC curve of P(DSP-DAEP).
Fig. S7. $^1$H NMR spectrum of P(DSP-DAEP) in D$_2$O.
Scheme S1. The chemical structure of FAM-labeled P(DSP-DAEP).

**Fig. S8.** $^1$H NMR spectrum of FAM-P(DSP-DAEP) in D$_2$O.
Quantification of reductive degradation of polymer P(DSP-DAEP)

The disappearance of the methylene $a_1$ peak (δ 2.68 ppm) and appearance of the $a_2$ (δ 2.48 ppm) peak was quantified by using $^1$H NMR in comparison with the original polymer.

Scheme S2. Polymer degradation upon the ascorbic acid reduction.

Fig. S9. Stacked $^1$H NMR spectrum of P(DSP-DAEP) with the ascorbic acid for various periods of incubation time at 37 °C.
**Scheme S3.** DSP degradation upon the ascorbic acid reduction.

**Fig. S10.** Stacked $^1$H NMR spectrum of DSP with the ascorbic acid for various periods of incubation time at 37 °C.
**Electrochemistry**

**Fig. S11.** Plot of reduction peak potential maxima of P(DSP-DAEP) at pH 7.4 as a function of scan rate.

**Fig. S12.** Plot of reduction peak potential maxima of P(DSP-DAEP) at pH 6.0 as a function of scan rate.
Fig. S13. Cell viability assays of DSP and P(DSP-DAEP) in Saos-2, U-2OS, A549 and HeLa cells.
Fig. S14. Intracellular Pt amount of DSP and P(DSP-DAEP) in HeLa at 20 μM and 60 μM based on Pt at 37 °C incubated for 3 h.

Fig. S15. Cell viability assay of DAEP in HeLa for 72 h.
Fig. S16. $^1$H NMR spectrum of mPEG-$b$-PpY in $D_2O$.

Table S1 Size and zeta potential of Pt-PIC with different feeding ratio of P/Pt

<table>
<thead>
<tr>
<th>P/Pt</th>
<th>Size (nm)</th>
<th>Zeta potential (mV)</th>
<th>Drug loading (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3:1</td>
<td>213</td>
<td>-72</td>
<td>13.1</td>
</tr>
<tr>
<td>2:1</td>
<td>178</td>
<td>-71</td>
<td>17.3</td>
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<tr>
<td>1:1</td>
<td>250</td>
<td>-23</td>
<td>21.8</td>
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</tbody>
</table>

Table S2. Size, zeta potential, and polydispersity index of Pt-PIC, ALP-treated Pt-PIC and ALP-treated mPEG-$b$-PpY.

<table>
<thead>
<tr>
<th></th>
<th>Pt-PIC</th>
<th>ALP-treated Pt-PIC</th>
<th>ALP-treated mPEG-$b$-PpY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eff.Diam.$^a$ (nm)</td>
<td>177.9</td>
<td>56.4</td>
<td>61.7</td>
</tr>
<tr>
<td>PDI$^b$</td>
<td>0.36</td>
<td>0.34</td>
<td>0.33</td>
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<tr>
<td>Zeta potential (mV)</td>
<td>-71.2</td>
<td>-28.7</td>
<td>-36.3</td>
</tr>
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</table>

Dephosphorylation process of mPEG-PpY and Pt-PIC with ALP measured by $^{31}$P NMR

Fig. S17. Stacked $^{31}$P NMR spectrum of Pt-PIC with the treatment of ALP for various periods of incubation time at 37 °C.
Fig. S18. The ALP expression levels of Saos-2 and U-2OS analyzed by flow cytometry assay.
Fig. S19. Cytotoxicity of mPEG-b-PpY.
**Fig. S20.** In vitro cytotoxicity of P(DSP-DAEP) and Pt-PIC in Saos-2 (ALP positive) and U-2OS (ALP negative) cell lines.