Supporting information for

Versatile multicompartment nanoparticles constructed with two thermo-responsive, pH-responsive and hydrolytic diblock copolymers

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1. Experimental Section

1.1 Synthesis of macro-RAFT agents

The macro-RAFT agent of PNASME_{153}-TTC was prepared by RAFT polymerization under [NASME]₀:[DDMAT]₀:[AIBN]₀ = 800:4:1 in 1,4-dioxane at 70 °C for 12 h. Into a Schlenk flask with a magnetic bar, NASME (1.57 g, 10.00 mmol), DDMAT (18.23 mg, 0.050 mmol), 1,3,5-trioxane (internal standard, 90.00 mg, 1.00 mmol), and AIBN (2.05 mg, 0.0125 mmol) dissolved in 1,4-diethylene dioxide (3.18 g, 3.06 mL) were added. The oxygen in flask content was excluded with high-purity argon at 0 °C, and then the polymerization was initiated at 70 °C under magnetically stirring. After 12 h, the polymerization was inhibited by rapid cooling upon immersion of the flask in iced water (-20 °C) and a monomer conversion of 76.5% was obtained. The monomer conversion was determined with ^1H NMR analysis by comparing the integral areas of the monomer protons of C=C-H at δ = 5.60-5.80 ppm with that of the 1,3,5-trioxane internal standard at δ = 5.10-5.20 ppm. The synthesized polymer was purified by three precipitation-filtration cycles in cold diethyl ether, and was dried under vacuum at room temperature overnight to
afford a pale yellow powder of PNASME\textsubscript{153}-TTC ($M_{n,th} = 24.3$ kg/mol, $M_{n,GPC} = 23.7$ kg/mol, $D = 1.22$).

A similar procedure of RAFT polymerization was also employed to prepare the macro-RAFT agent of P4VP\textsubscript{133}-TTC under [4VP]\textsubscript{0}:[DDMAT]\textsubscript{0}:[AIBN]\textsubscript{0} = 800:4:1 in ethanol at 70 °C. After 12h, a monomer conversion of 66.5% was determined by $^1$H NMR analysis. The synthesized polymer was purified by three precipitation-filtration cycles in cold diethyl ether, and then dried under vacuum at 25 °C overnight to afford a light pink powder of P4VP\textsubscript{133}-TTC ($M_{n,th} = 14.3$ kg/mol, $M_{n,GPC} = 13.2$ kg/mol, $D = 1.17$).

1.2 Synthesis of nanoassemblies formed by individual block copolymers

The PNASME\textsubscript{153-}b-PS or P4VP\textsubscript{133-}b-PS nano-assemblies were prepared by dispersion RAFT polymerization employing PNASME\textsubscript{153}-TTC or P4VP\textsubscript{133}-TTC as macro-RAFT agent under [St]\textsubscript{0}:[macro-RAFT]\textsubscript{0}:[AIBN]\textsubscript{0} = 900:3:1 similarly with the dispersion RAFT polymerization employing two macro-RAFT agents introduced in Section 2.3. The obtained diblock copolymers are PNASME\textsubscript{153-}b-PS\textsubscript{279} (T\textsubscript{153}S\textsubscript{279}, $M_{n,th} = 53.4$ kg/mol, $M_{n,GPC} = 50.2$ kg/mol, $D = 1.29$) and P4VP\textsubscript{133-}b-PS\textsubscript{292} (H\textsubscript{133}S\textsubscript{292}, $M_{n,th} = 44.6$ kg/mol, $M_{n,GPC} = 42.3$ kg/mol, $D = 1.21$).

2. Equations and Tables

\[
M_{n,th} = \frac{[\text{monomer}]_0 \times M_{\text{monomer}}}{[\text{RAFT}]_0} \times \text{Conversion} + M_{n,\text{RAFT/macro-RAFT}} \quad (\text{S1})
\]

where [monomer]\textsubscript{0} and [RAFT]\textsubscript{0} represent the concentration of the fed monomer and the RAFT agent, $M_{\text{monomer}}$ is the molar mass of the monomer, $M_{n,\text{RAFT/macro-RAFT}}$ is the molar mass of RAFT/macro-RAFT agent, and the monomer Conversion is determined by $^1$H
NMR analysis by comparing the integral areas of the monomer protons of C=C-H at δ = 5.60-5.80 ppm with those of the 1,3,5-trioxane internal standard at δ = 5.10-5.20 ppm.

The $M_{n,\text{NMR}}$ of separated diblock copolymers, i.e., PNASME-b-PS (eq. S2) and P4VP-b-PS (eq. S2) was calculated with the ratio of two blocks by $^1$H NMR analysis (2.6-3.2 ppm corresponding to methyl of the PNASME block and 6.2-7.3 ppm corresponding to phenyl group of the PS block, and 8.0-8.4 ppm corresponding to pyridyl of the P4VP block).

$$M_{n,\text{NMR}} = DP_{\text{PS}} \times M_{\text{St}} + M_{\text{PNASME-TC}} = \frac{I_{2.6-3.2} \times \frac{1}{3}}{I_{8.0-8.4} \times \frac{1}{6}} \times DP_{\text{PNASME-TC}} \times M_{\text{St}} + M_{\text{PNASME-TC}} \quad (\text{S2})$$

$$M_{n,\text{NMR}} = DP_{\text{PS}} \times M_{\text{St}} + M_{\text{P4VP-TC}} = \frac{I_{6.2-7.3} \times \frac{1}{7}}{I_{8.0-8.4} \times \frac{1}{6}} \times DP_{\text{P4VP-TC}} \times M_{\text{St}} + M_{\text{P4VP-TC}} \quad (\text{S3})$$

**Table S1.** Summary of the synthesized MCBNs.

<table>
<thead>
<tr>
<th>Figures</th>
<th>MCBNs a</th>
<th>[H]o/[T]o:</th>
<th>Conv. b</th>
<th>$M_{n,\text{NMR}}$(kg/mol) c</th>
<th>$M_{n,\text{GPC}}$(kg/mol) / $\bar{D}$ d</th>
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</thead>
<tbody>
<tr>
<td>4B/5B</td>
<td>T$<em>{153S260}$/$H</em>{133S260}$</td>
<td>1800:3:3:1</td>
<td>86.7</td>
<td>50.6  43.9  43.1/1.37  45.2/1.25  40.7/1.21</td>
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<tr>
<td>4A</td>
<td>T$<em>{153S260}$/$H</em>{133S260}$</td>
<td>1800:4:2:1</td>
<td>87.2</td>
<td>51.4  43.4  43.7/1.40  45.5/1.22  39.8/1.19</td>
<td></td>
</tr>
<tr>
<td>4C</td>
<td>T$<em>{153S264}$/$H</em>{133S264}$</td>
<td>1800:2:4:1</td>
<td>88.3</td>
<td>50.3  44.5  44.2/1.42  46.6/1.24  41.7/1.28</td>
<td></td>
</tr>
<tr>
<td>5A</td>
<td>T$<em>{153S90}$/$H</em>{133S90}$</td>
<td>600:3:3:1</td>
<td>90.1</td>
<td>33.6  23.8  27.4/1.36  30.9/1.18  21.2/1.15</td>
<td></td>
</tr>
<tr>
<td>5C</td>
<td>T$<em>{153S390}$/$H</em>{133S390}$</td>
<td>3000:3:3:1</td>
<td>78.2</td>
<td>64.6  57.1  52.3/1.44  58.1/1.31  49.8/1.27</td>
<td></td>
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<tr>
<td>9A-B</td>
<td>T$<em>{153S260}$/$H</em>{133S260}$</td>
<td>1800:3:3:1</td>
<td>86.7</td>
<td>48.5  43.9  42.7/1.41  44.1/1.20  39.8/1.17</td>
<td></td>
</tr>
</tbody>
</table>

a T, H, S and T’ denotes PNASME, P4VP, PS and PNAS block, respectively, b the monomer conversion was determined by $^1$H NMR analysis, c the molecular weight by NMR analysis according to eqs. S2 and S3, d the polymer molecular weight and $\bar{D}$ ($M_w/M_n$) by GPC analysis, e TS denotes the separated PNASME-b-PS diblock copolymer or the hydrolytic PNAS-b-PS diblock copolymer, f HS denotes the separated P4VP-b-PS diblock copolymer. Note: the MCBNs of T$_{153S260}$/$H_{133S260}$ was prepared with hydrolyzing from T$_{153S260}$/$H_{133S260}$. 

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3. Supplementary Figures

**Figure S1.** TEM images of the non-stained nanoparticles of PNASME$_{153}$-b-PS$_{279}$ (T$_{153}$S$_{279}$, A), P4VP$_{133}$-b-PS$_{292}$ (H$_{133}$S$_{292}$, B) dispersed in ethanol/water (80/20 w/w) prepared via dispersion RAFT polymerization employing individual macro-RAFT agents and the PNASME$_{153}$-b-PS$_{260}$/P4VP$_{133}$-b-PS$_{260}$ nanoparticles (T$_{153}$S$_{260}$/H$_{133}$S$_{260}$, C) prepared employing two macro-RAFT agents.

**Figure S2.** Temperature-dependent transmittance of 0.01 wt% PNASME$_{153}$-TTC aqueous solution.
Figure S3. DSC thermograms of the PNASME₁₅₃/P₄VP₁₃₃ (1/1 w/w) blends (A), and PNAS₁₅₃-b-PS₂₆₀/P₄VP₁₃₃-b-PS₂₆₀ (B) obtained from hydrolysis of PNASME₁₅₃-b-PS₂₆₀/P₄VP₁₃₃-b-PS₂₆₀, the separated diblock copolymer of P₄VP₁₃₃-b-PS₂₆₀ (C) and PNAS₁₅₃-b-PS₂₆₀ (D). Note: The glass transition temperature ($T_g$) of PNASME₁₅₃ is about 102.1 °C and the $T_g$ of P₄VP₁₃₃ is about 141.4 °C.

Figure S4. $^1$H NMR spectra of the PNASME₁₅₃-b-PS₂₆₀/P₄VP₁₃₃-b-PS₂₆₀ nanoparticles before hydrolysis (A) and the PNAS₁₅₃-b-PS₂₆₀/P₄VP₁₃₃-b-PS₂₆₀ nanoparticles after hydrolysis (B). Note: the signal of H₂O (3.33 ppm) in DMSO-$d_6$ was inhibited by water suppression experiment.
Figure S5. pH dependence of Zeta-potentials of the PNAS$_{153}$-b-PS$_{260}$/P4VP$_{133}$-b-PS$_{260}$ nanoparticles in aqueous solution at pH = 12.0, pH = 2.0 and pH = 6.5, respectively. Insets: the schematic structures of nanoparticles in aqueous solution are at pH = 2.0 and pH = 6.5, respectively.