Supporting Information

Esterase-Responsive Polymeric Prodrug-Based Tumor Targeting Nanoparticles for Improved Anti-Tumor Performance against Colon Cancer

Gang Pan¹, #, Yi-jie Bao¹, #, Jie Xu¹, #, Tao Liu², Cheng Liu², Yan-yan Qiu², Xiao-jing Shi¹, Hui Yu¹, Ting-ting Jia³, Xia Yuan³, Ze-ting Yuan², Pei-hao Yin¹,4*, and Yi-jun Cao¹,*

¹Department of General Surgery, Putuo Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai, 200062, China
²Centralab, Putuo Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai, 200062, China
³Department of Pharmacy, Putuo Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai, 200062, China
⁴Interventional Cancer Institute of Chinese Integrative Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai, 200062, China

#These authors contributed equally to this work
* To whom correspondence should be addressed. E-mail: yinpeihao1975@hotmail.com caoyjxw@126.com
Table S1. Molecular parameters of polymers used in this study.

<table>
<thead>
<tr>
<th>Sample</th>
<th>$M_n$ (g/mol)$^a$</th>
<th>$D_m$$^a$</th>
<th>$M_n$ (g/mol)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>P(OEGMA$<em>{0.45}$-co-BSMA$</em>{0.55}$)$_2$</td>
<td>25,000</td>
<td>1.29</td>
<td>24,800</td>
</tr>
<tr>
<td>P(OEGMA$<em>{0.45}$-co-BUF$</em>{0.46}$-co-NHS$_{0.09}$)$_2$</td>
<td>37,700</td>
<td>1.21</td>
<td>37,700</td>
</tr>
<tr>
<td>P(OEGMA$<em>{0.45}$-co-BUF$</em>{0.46}$-co-NHS$<em>{0.062}$-co-RGD$</em>{0.028}$)$_2$</td>
<td>38,900</td>
<td>1.32</td>
<td>38,900</td>
</tr>
<tr>
<td>P(OEGMA$<em>{0.45}$-co-BUF$</em>{0.46}$-co-NHS$<em>{0.048}$-co-RGD$</em>{0.028}$-co-Cy$_{5.0014}$)$_2$</td>
<td>39,000</td>
<td>1.31</td>
<td>39,500</td>
</tr>
<tr>
<td>P(OEGMA$<em>{0.45}$-co-BUF$</em>{0.46}$-co-NHS$<em>{0.076}$-co-Cy$</em>{5.0014}$)$_2$</td>
<td>39,100</td>
<td>1.30</td>
<td>38,400</td>
</tr>
</tbody>
</table>

$a$ Determined by GPC using DMF as the eluent (1.0 mL/min). $^b$ Calculated from $^1$H NMR results.
Fig. S1. $^1$H NMR spectrum of tert-butyl-3-((2-hydroxyethyl)thio)propanoate in CDCl$_3$. 
Fig. S2. $^1$H NMR spectrum of 2-((3-(tert-butoxy)-3-oxopropyl)thio)ethyl methacrylate in CDCl$_3$. 
Fig. S3. $^{13}$C NMR spectrum of 2-((3-(tert-butoxy)-3-oxopropyl)thio)ethyl methacrylate in CDCl$_3$. 
**Fig. S4.** ESI-Mass spectra of (a) 2-((3-(tert-butoxy)-3-oxopropyl)thio)ethyl methacrylate (m/z 188, calculated for C_{9}H_{10}O_{2}S: 188) and (b) 3-((2-(methacryloyloxy)ethyl)thio)propanoic acid (BSMA) (m/z 132, calculated for C_{5}H_{8}O_{2}S: 132).
Fig. S5. $^1$H NMR spectrum of BSMA in CDCl$_3$. 
Fig. S6. $^{13}$C NMR spectrum of BSMA in CDCl$_3$. 
Fig. S7. $^1$H NMR spectrum of P(OEGMA-co-BSMA) in CDCl$_3$. 
Fig. S8. $^1$H NMR spectrum of P(OEGMA-co-BUF) in DMSO-$d_6$. 
Fig. S9. $^1$H NMR spectrum of P(OEGMA-co-BUF-co-RGD) in DMSO-$d_6$. 
Fig. S10. Fluorescence emission spectrum recorded for the aqueous micellar solution of P(OEGMA-co-BUF-co-RGD-co-Cy5) ([Cy5] = 3.0 × 10^{-6} M; \lambda_{ex} = 633 \text{ nm}; \text{ slit widths: Ex. 5 nm, Em. 5 nm}).
Fig. S11. Typical confocal microscopy fluorescence images recorded for LoVo cells after incubating at 37 °C with P(OEGMA-co-BUF-co-RGD-co-Cy5) ([Cy5] = 3.0 × 10^{-6} M) for 4 h (a) without and (b) with an excess of free RGD (20-fold equivalent of RGD in P(OEGMA-co-BUF-co-RGD-co-Cy5)) to block RGD-mediated endocytosis of nanoparticles.