

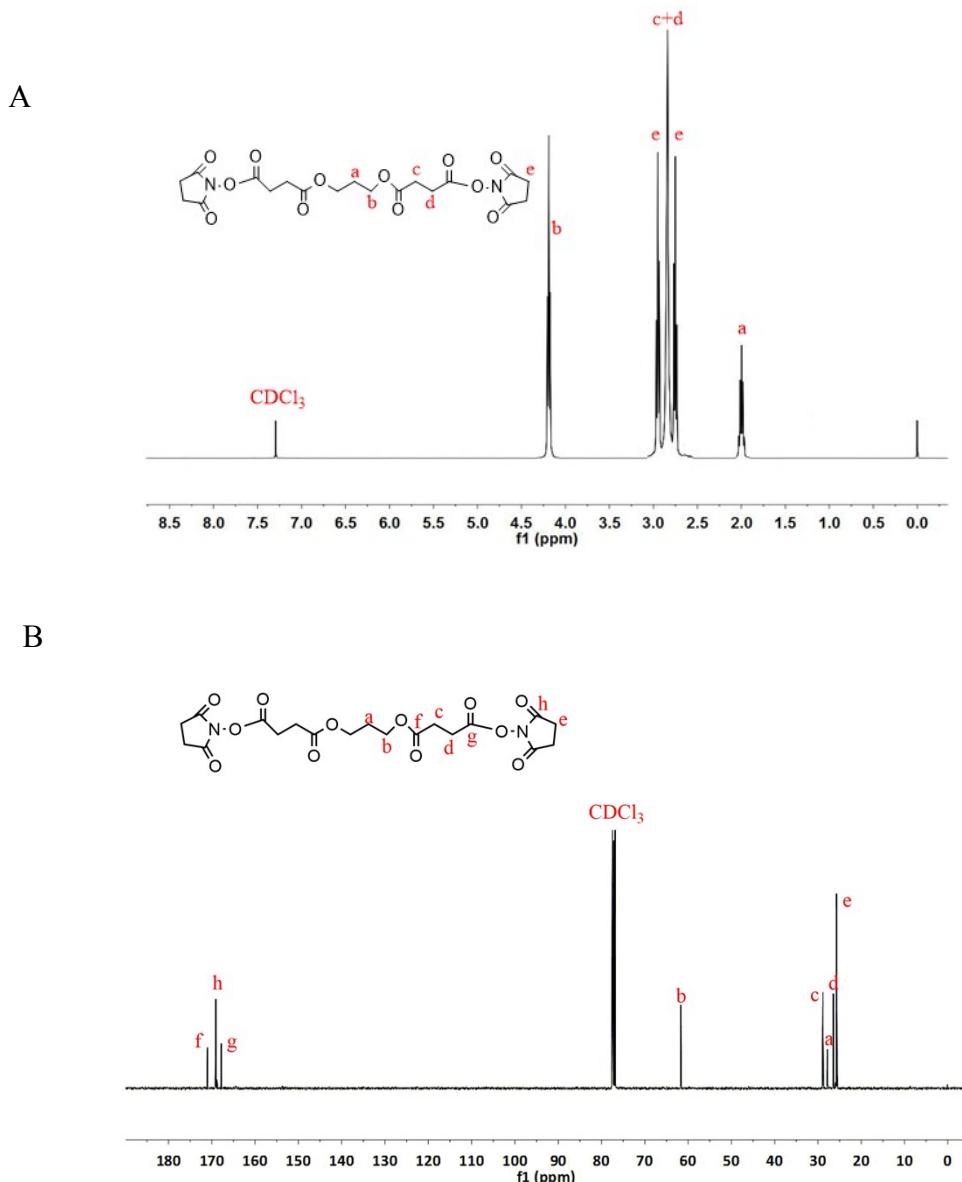
**† Electronic Supplementary Information (ESI)**

**Tunable dynamic fluorinated poly(ortho ester)-based drug carriers for greatly enhanced chemotherapeutic efficacy**

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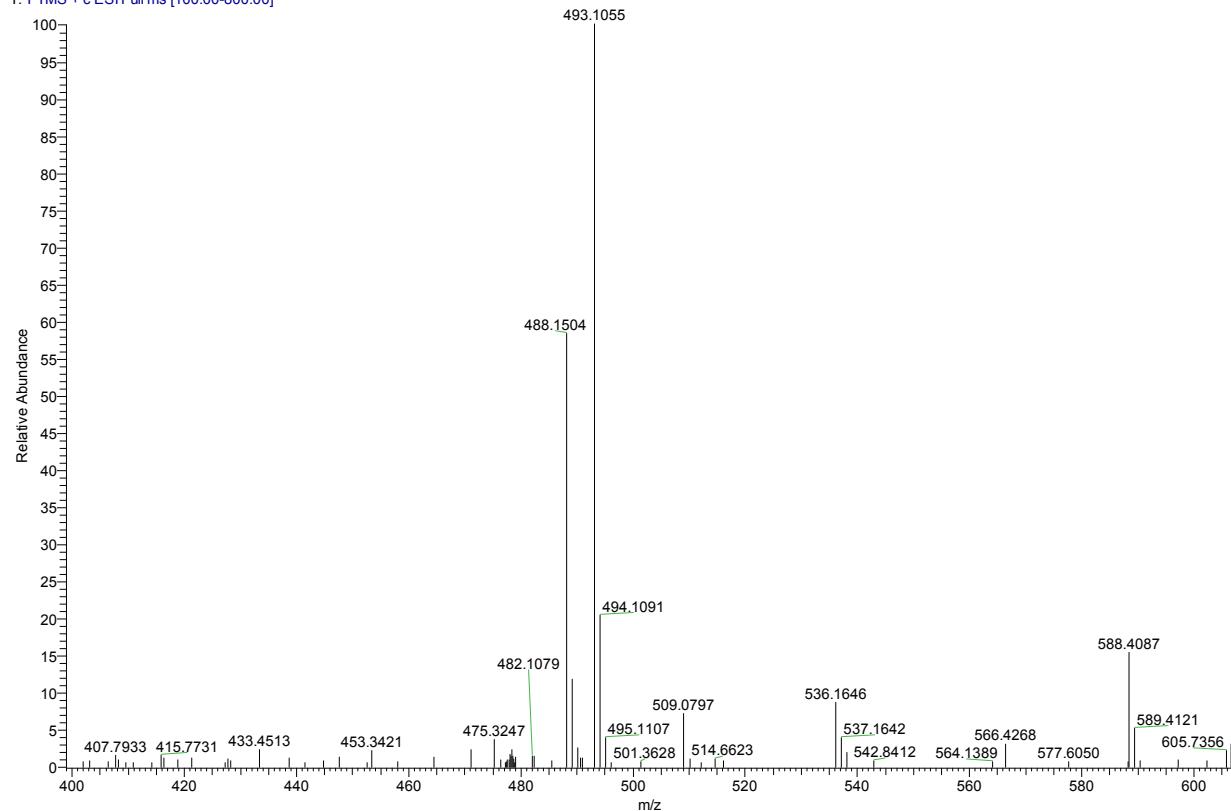
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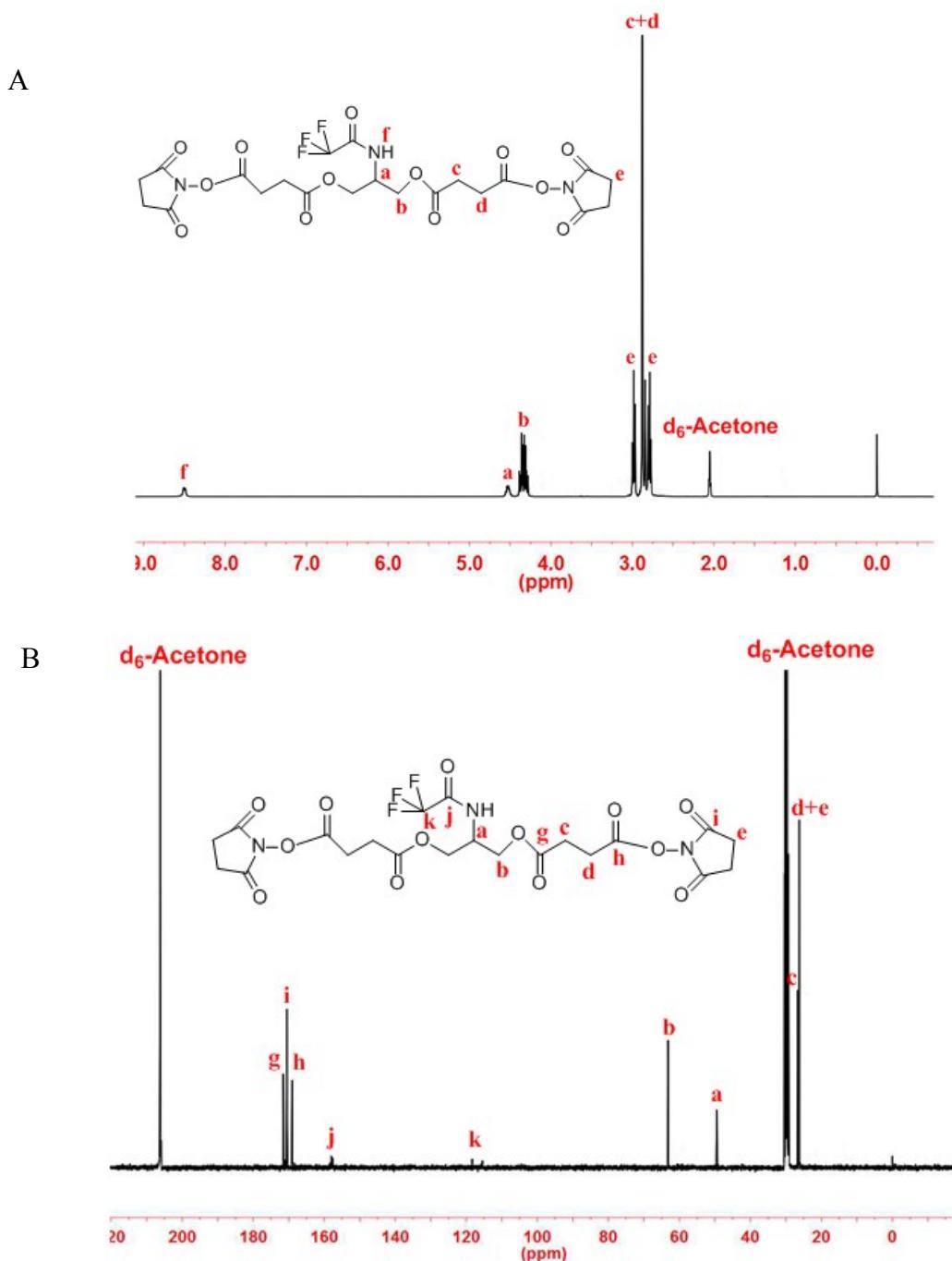


**Fig. S1**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectra of bis(2,5-dioxopyrrolidin-1-yl) O,O'- (propane-1,3-diyl) disuccinate in  $\text{CDCl}_3$  recorded on a Bruker AM-400 MHz spectrometer at 25°C (ppm).

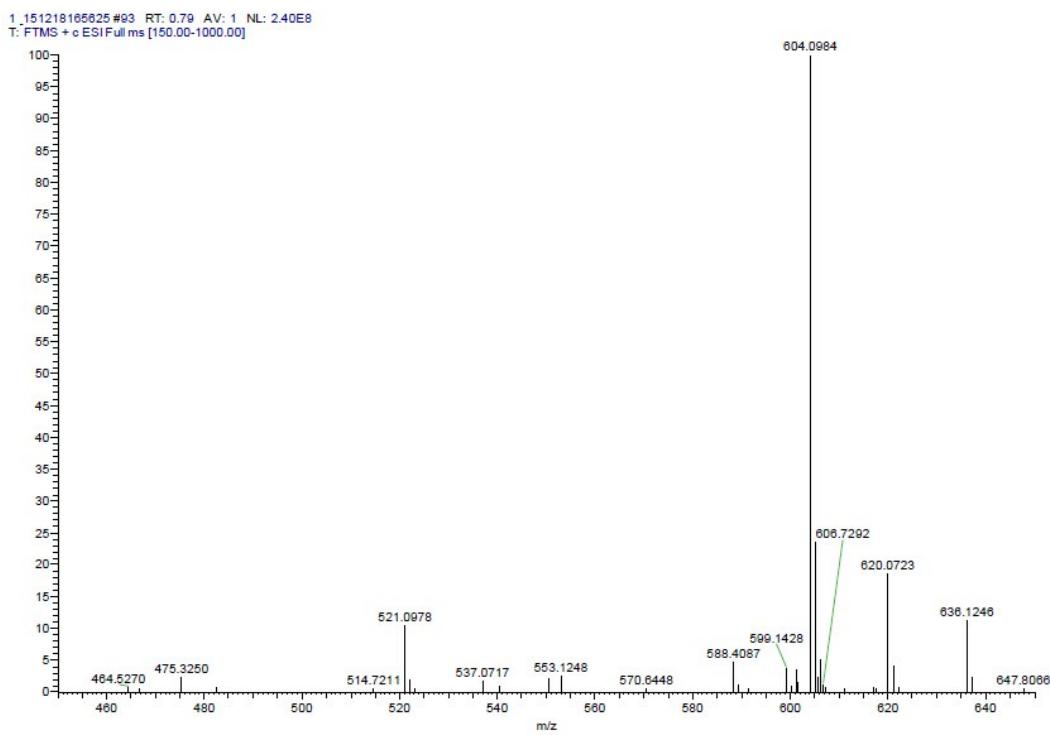
C3 #19 RT: 0.20 AV: 1 NL: 6.61E6  
T: FTMS + c ESI Full ms [100.00-800.00]



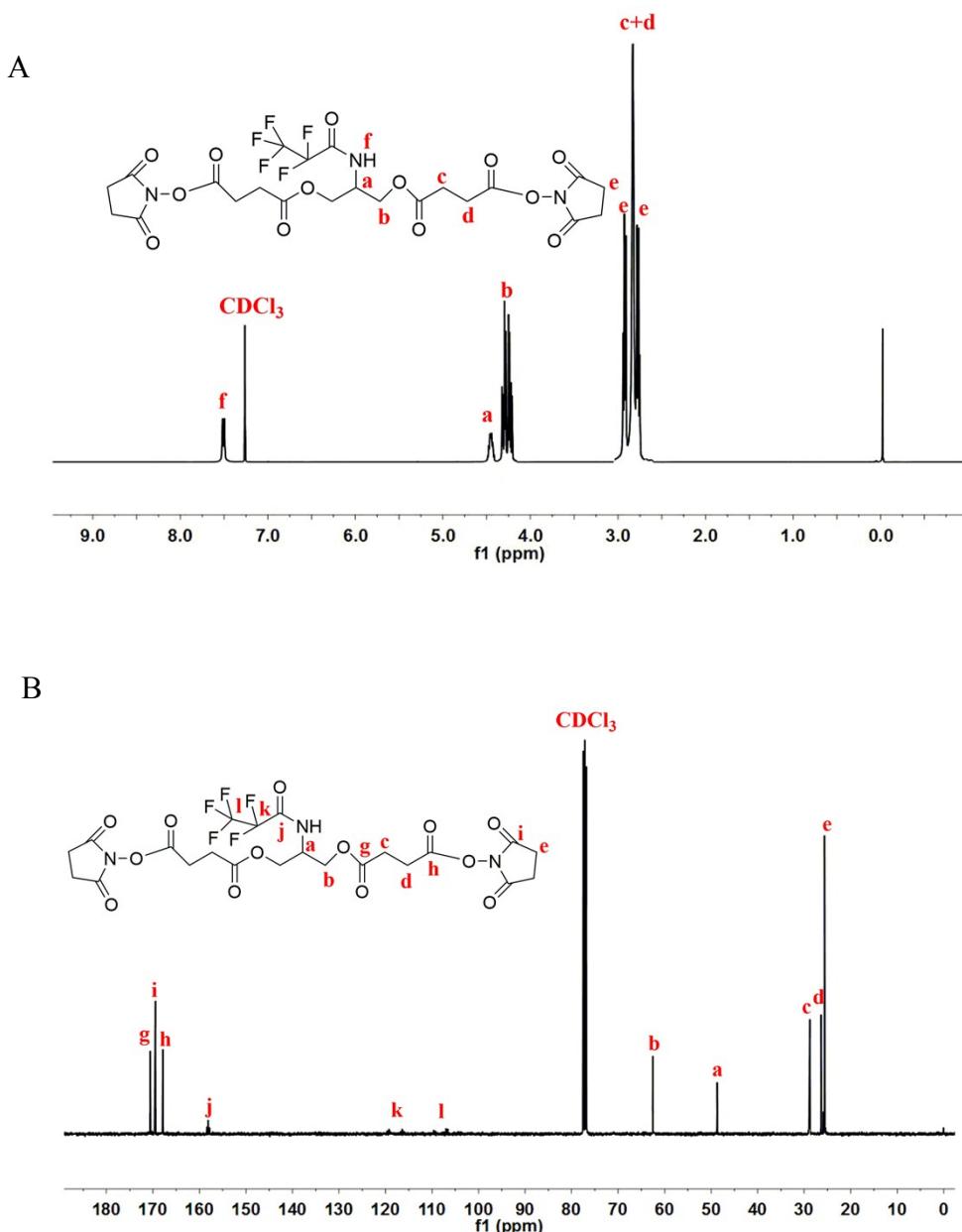
**Fig. S2** Mass spectrum of bis(2,5-dioxopyrrolidin-1-yl) O,O'-(propane-1,3-diyl) disuccinate recorded on a LTQ Orbitrap XL high-resolution mass spectrometer. ESI-MS Calcd for ( $C_{19}H_{22}N_2O_{12}$ ): 470.1; found m/z: 493.1 ( $M+ Na^+$ ).



**Fig. S3**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectrum of bis(2,5-dioxopyrrolidin-1-yl) O,O'-(2-(2,2,2-trifluoroacetamido)propane-1,3-diyl) disuccinate in  $\text{d}_6$ -Acetone recorded on a Bruker AM-400 MHz spectrometer at 25°C (ppm).

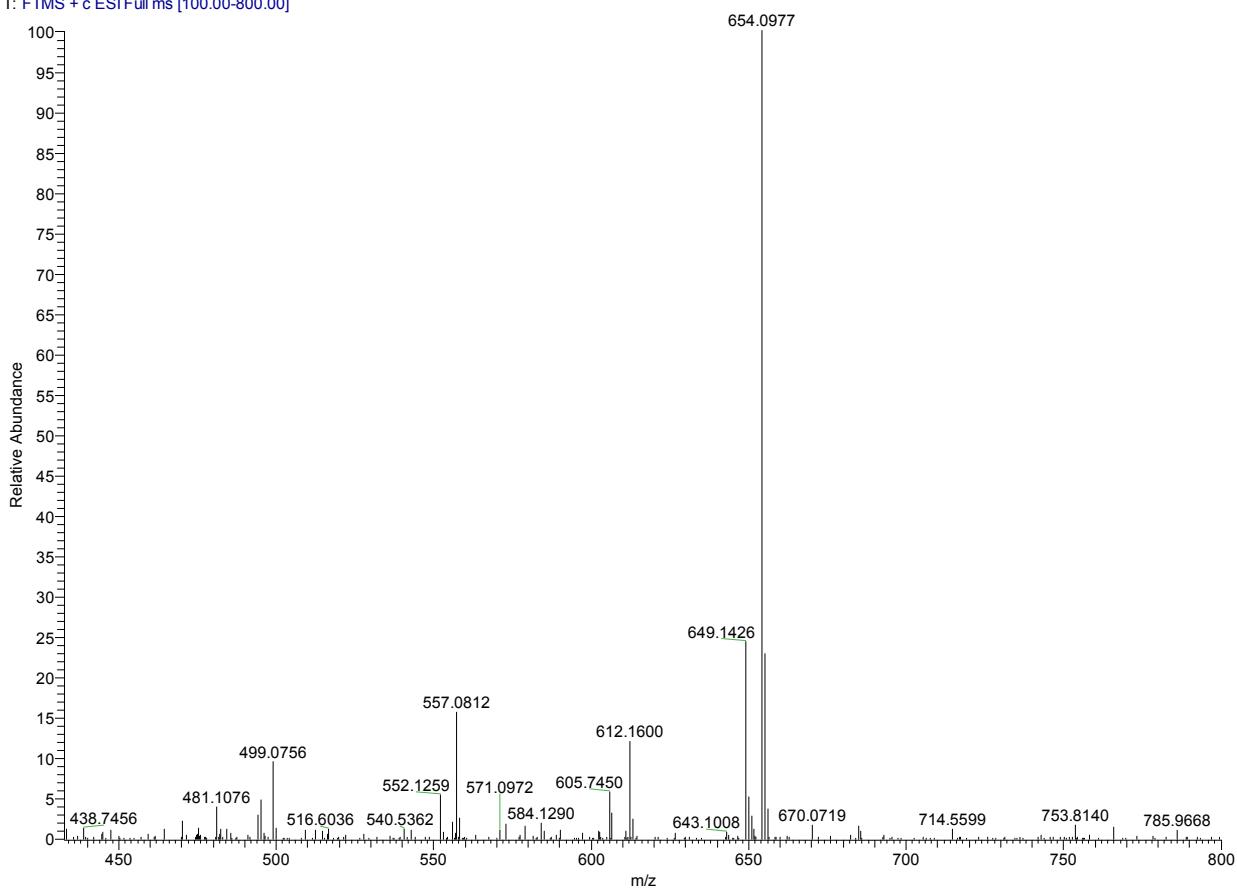


**Fig. S4** Mass spectrum of bis(2,5-dioxopyrrolidin-1-yl) O,O'-(2-(2,2,2-trifluoroacetamido)propane-1,3-diyl) disuccinate recorded on a LTQ Orbitrap XL high-resolution mass spectrometer. ESI-MS Calcd for ( $C_{21}H_{22}F_3N_3O_{13}$ ): 581.1; found m/z: 604.1 ( $M + Na^+$ ).

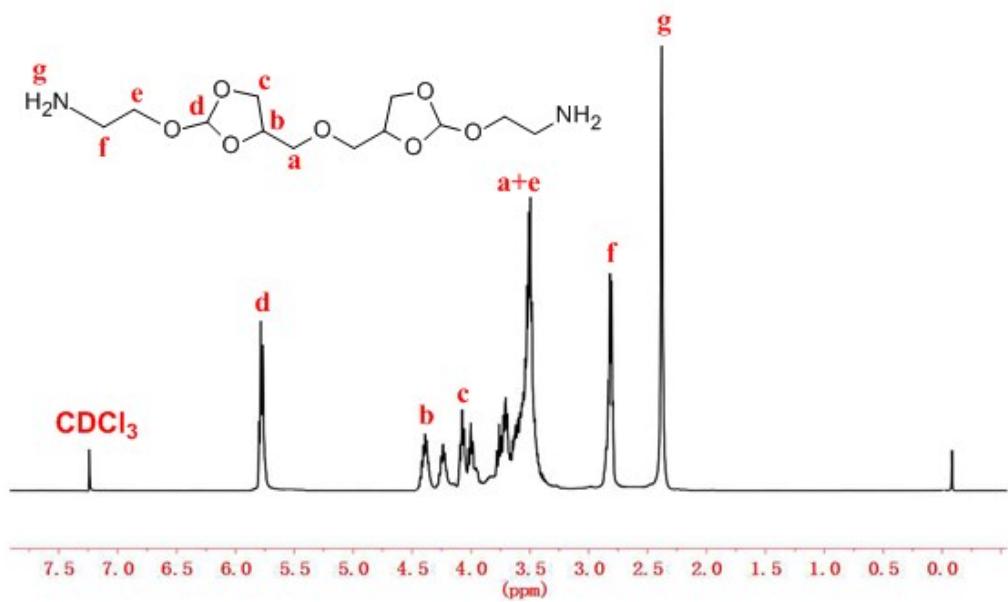


**Fig. S5**  $^1\text{H}$  NMR (A) and  $^{13}\text{C}$  NMR (B) spectrum of bis(2,5-dioxopyrrolidin-1-yl) O,O'-(2-(2,2,3,3,3-pentafluoropropanamido)propane-1,3-diyl) disuccinate in  $\text{CDCl}_3$  recorded on a Bruker AM-400 MHz spectrometer at  $25^\circ\text{C}$  (ppm).

F5 #11-15 RT: 0.14-0.19 AV: 5 NL: 5.50E7  
T: FTMS + c ESI Full ms [100.00-800.00]



**Fig. S6** Mass spectrum of bis(2,5-dioxopyrrolidin-1-yl) O,O'-(2-(2,2,3,3,3-pentafluoropropanamido)propane-1,3-diyl) disuccinate recorded on a LTQ Orbitrap XL high-resolution mass spectrometer. ESI-MS Calcd for ( $C_{22}H_{22}F_5N_3O_{13}$ ): 631.1; found m/z: 654.1 ( $M + Na^+$ ).



**Fig. S7**  $^1\text{H}$  NMR spectrum of 2,2'-(4,4'-oxybis(methylene)) bis(1,3-dioxolane-4,2-diyl) bis(Oxy)) diethanamine in  $\text{CDCl}_3$  recorded on a Bruker AM-400 MHz spectrometer at 25°C.

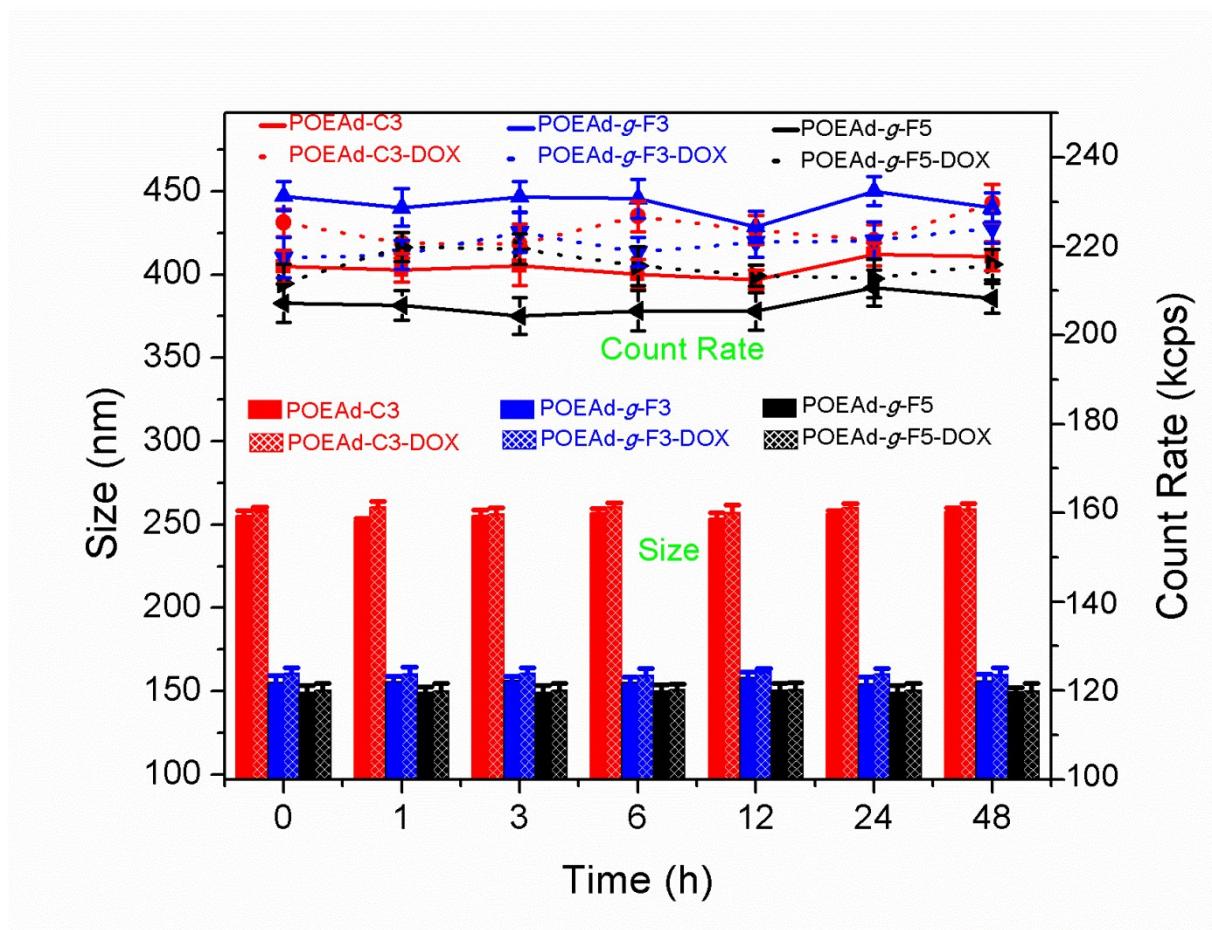
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**Table S1** Characterization of copolymers.

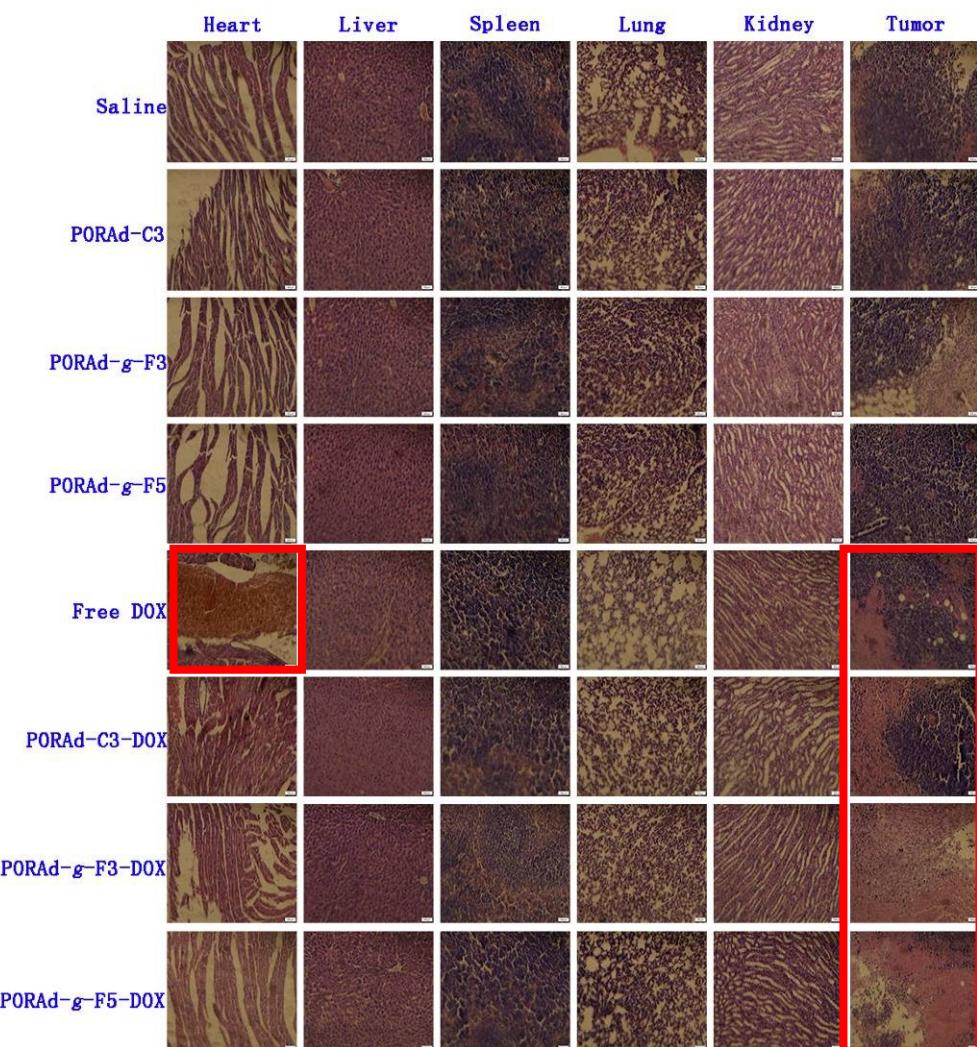
Polymer	Yield[%]	M <sub>n</sub> [×10 <sup>4</sup> ]	M <sub>w</sub> [×10 <sup>4</sup> ]	PDI
POEAd-C3	84.2	1.2	1.9	1.59
POEAd- <i>g</i> -F3	83.0	1.4	2.0	1.45
POEAd- <i>g</i> -F5	82.5	1.5	2.2	1.49

**Table S2** Drug loading efficiency (DLE), drug loading content (DLC) of nanospheres-DOX, and sizes of blank nanospheres and nanospheres-DOX.

Materials	DLE[%]	DLC[%]	Size[nm]	PDI
POEAd-C3	-	-	255.5±0.4	0.115
POEAd- <i>g</i> -F3	-	-	155.2±0.6	0.108
POEAd- <i>g</i> -F5	-	-	149.1±0.7	0.124
POEAd-C3-DOX	58.7	13.5	258.3±1.2	0.125
POEAd- <i>g</i> -F3-DOX	78.5	18.7	156.9±1.5	0.137
POEAd- <i>g</i> -F5-DOX	88.3	24.2	150.6±0.8	0.104



**Fig. S8** Particle sizes and count rates of both empty and DOX-loaded nanospheres vs time measured by DLS in the presence of sodium dodecyl sulfate (SDS).



**Fig. S9** Images of the histological sections of H22 grafted tumors; Scale bar = 500  $\mu\text{m}$ .