Supporting Information

Bottlebrush-Architectured Dextran Polyprodrug as an Acidity-

Responsive Vector for Enhanced Chemotherapy Efficiency

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Figure S1. Synthetic route of pH-responsive prodrug copolymer DEX-P(OEGMA)-*b*-P(MGMA-DOX) (DOM@DOX).



Figure S2. ¹H NMR spectrum of DEX-Br initiator in CDCl₃.



Figure S3. ¹H NMR spectrum of DEX₁₀₀₀-POEGMA polymer in CDCl₃.



Figure S4. ¹H NMR spectrum of DEX₁₀₀₀-POEGMA-*b*-PMGMA in CDCl₃.



Figure S5. ¹H NMR spectrum of DOM₁₀₀₀@hydrazide in DMSO-d₆.



Figure S6. ¹H NMR spectrum of DOM₁₀₀₀@DOX in DMSO-d₆.



Figure S7.GPC traces of DEX₁₀₀₀-POEGMA, DEX₁₀₀₀-POEGMA-*b*-PMGMA and DEX₅₀₀₀@POEGMA, DEX₅₀₀₀@POEGMA-*b*-PMGMA.



Figure S8. The fluorescence intensity ratio I_3/I_1 of pyrene as a function of DOM₁₀₀₀@DOX and DOM₅₀₀₀@DOX concentration. The critical micell concentration (CMC) in aqueous are measured as about 6.8 µg/mL and 12.5 µg/mL for DOM₁₀₀₀@DOX and DOM₅₀₀₀@DOX.



Figure S9. The fluorescence intensity curve of HeLa cells after incubated with $DOM_{1000}DOX$ and $DOX_{5000}@DOX$ for 2h and 6h respectively by CLSM.



Figure S10. Flow cytometry dot plots for HeLa cells treated with DOM₁₀₀₀@DOX (A) and DOM₅₀₀₀@DOX (B) for 0.5h, 2h, 4h and 6h respectively.



Figure S11. Time dependent DOX concentration curve after intravenous administration of Free DOX, DOM_{1000} @DOX and DOM_{5000} @DOX *in vivo*. Data are reported as mean ± s.d. (n = 3).

Polymer ^a	$M_{n, GPC}^{b}$ (g mol ⁻¹)	Mw/Mn ^c	D ^d (water)	LC °(wt%)
DEX ₁₀₀₀ -P(OEGMA) ₄	28500	1.77	_	_
DEX ₅₀₀₀ -P(OEGMA) ₇	50100	1.56	_	_
DEX ₁₀₀₀ -P(OEGMA) ₄ -b- P(MGMA) ₈	30800	1.73	37.56	42.7±2.8
DEX ₅₀₀₀ -P(OEGMA) ₇ -b- P(MGMA) ₁₇	52300	1.63	49.26	48.1±2.9

Table S1. Structural information of the bottlebrush-architectured DOM copolymers and DOM@DOX.

^aThe degree of polymerization of OEGMA and MGMA were obtained from the ¹H NMR results; ^bNumber-average molecular weight, $M_{n,GPC}$ determined by GPC. ^cPolydispersity index, PDI determined by GPC. ^dHydrodynamic diameter of DOM@DOX in water were measured by DLS. ^eThe loading content (LC) of DOM@DOX were determined by fluorescence (FL) spectrophotometer, and the data are presented as means ± SD (n = 3).