Supporting Information

Hydrogen-Bonded Supramolecular Micelle-Mediated Drug Delivery
Enhances the Efficacy and Safety of Cancer Chemotherapy

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Scheme S1: Synthetic routes for BDAP-PEG.
Fig. S1: 500 MHz $^1$H NMR spectrum of dipropargyl PEG in deuterated chloroform (CDCl$_3$) at 25 °C.
**Fig. S2:** 500 MHz $^1$H NMR spectrum of BDAP-PEG in CDCl$_3$ at 25 °C.
Fig. S3: GPC traces of dipropargyl PEG and BDAP-PEG with DMF eluent at 50 °C.
Fig. S4: MALDI-TOF mass spectra of dipropargyl PEG and BDAP-PEG.
Fig. S5: 500 MHz $^1$H NMR spectra for BDAP-PEG in 1,1,2,2-tetrachloroethane-$d_2$ at various temperatures.
**Fig. S6:** Particle size distribution of blank and DOX-loaded BDAP-PEG micelles (DLC = 17.60 ± 1.5%) in water at 25 °C.

**Figure S7:** Digital photos for (a) blank and (b) DOX-loaded BDAP-PEG micelles in aqueous solution.
Fig. S8: *In vitro* cytotoxicity assay of BDAP-PEG micelles towards NIH/3T3 cells at 24 h.
Fig. S9: *In vitro* cytotoxicity of BDAP-PEG micelles towards HeLa cells at 24 h.
Fig. S10: CLSM images of HeLa cells incubated with DOX-loaded BDAP-PEG micelles (DLC = 17.60 ± 1.5%) for 6 h or 16 h at pH 7.4 and 37 °C. Micrographs of DOX-loaded micelles stained with the nuclear stain DAPI (top panel; blue), characteristic DOX fluorescence (middle panel; red) and merged images (lower panel). Scale bars are 20 μm for all images.
Fig. S11: Quantification of apoptosis by Annexin-V/PI double staining and flow cytometry. Dot plot diagrams of HeLa cells incubated with DOX-loaded BDAP-PEG (DLC = 17.60 ± 1.5%) for 1, 12 or 24 h at pH 6.5 and 37 °C.
In order to provide more detailed material properties, CMC and DLS measurements were employed to characterize the self-assembly behavior of difunctional hexyl-terminated PEG (BC6-PEG, Fig. S12) in water. Fig. S13 shows that aqueous BC6-PEG solution with a broad range of concentrations between 1 and $10^{-5}$ mg/mL did not exhibit a CMC transition. However, BDAP-PEG exhibited a clear CMC at 0.005 mg/mL, suggesting that the DAP moieties within BDAP-PEG significantly affected the amphiphilicity and molecular motion of the PEG backbone in water. DLS revealed that BC6-PEG did not exhibit micellar aggregates, whereas BDAP-PEG exhibited a mean hydrodynamic diameter of $53 \pm 15$ nm (Fig. S14), indicting introduction of DAP groups into the PEG chain ends facilitated the formation of nanosized micelles.

**Figure S12:** $^1$H NMR spectrum of BC6-PEG in CDCl$_3$.  

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**Figure S13:**
Figure S13: CMC determination for BC6-PEG and BDAP-PEG.

Figure S14: DLS analyses of 1.0 mg/mL solutions of BC6-PEG and BDAP-PEG in aqueous solution.