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Supporting Information

Aqueous seeded RAFT polymerization for the preparation of self-assemblies containing nucleobase analogues

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mDAP solubility tests.

The monomer (**mDAP**) solubility was tested in a range from 250 to 25 mg mL^{-1}, firstly in water, and then in mixtures water/dioxane (80:20 w/w), water/DMF (80:20 w/w), and water/ethanol (80:20 w/w). **mDAP** results insoluble in all of them for all the concentrations tested.

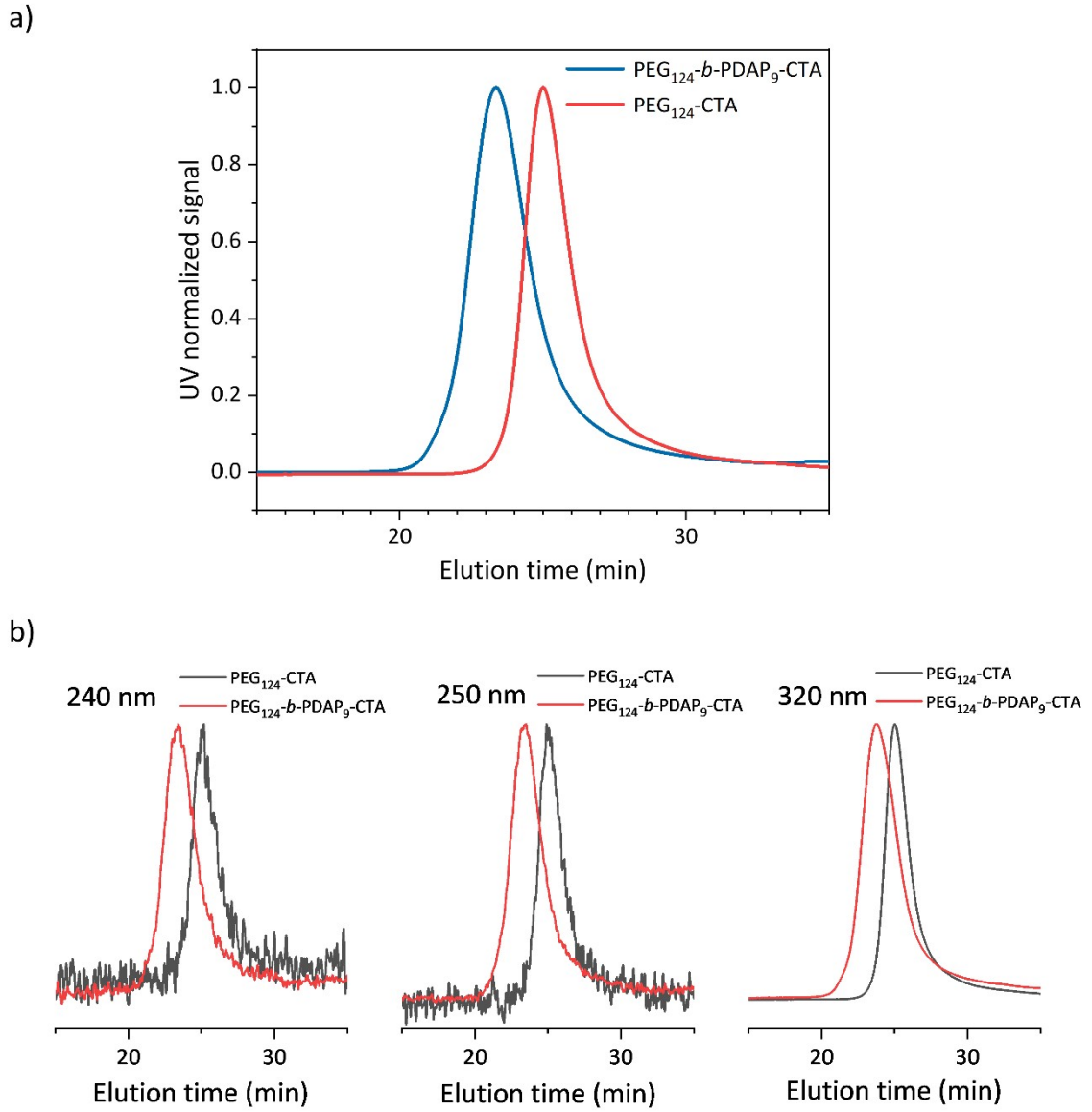

Fig. S1. (a) GPC chromatogram of **PEG_{124}-CTA** and **PEG_{124}-*b*-$PDAP_9$-CTA** recorded at 290 nm. (b) GPC chromatograms of **PEG_{124}-CTA** and **PEG_{124}-*b*-$PDAP_9$-CTA** recorded at different wavelengths (240 nm, 250 nm and 320 nm).

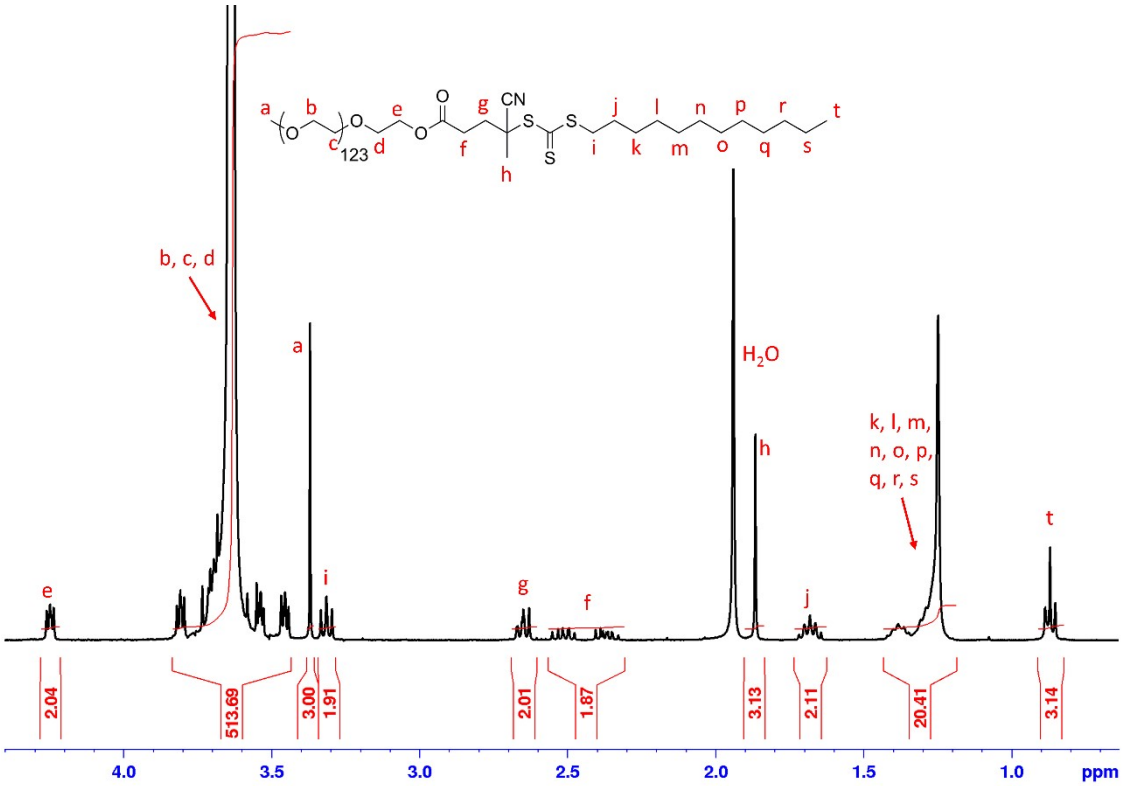

Fig. S2. ^{1}H NMR spectrum of **PEG$_{124}$-CTA** ($CDCl_3$, 400 MHz) δ (ppm).

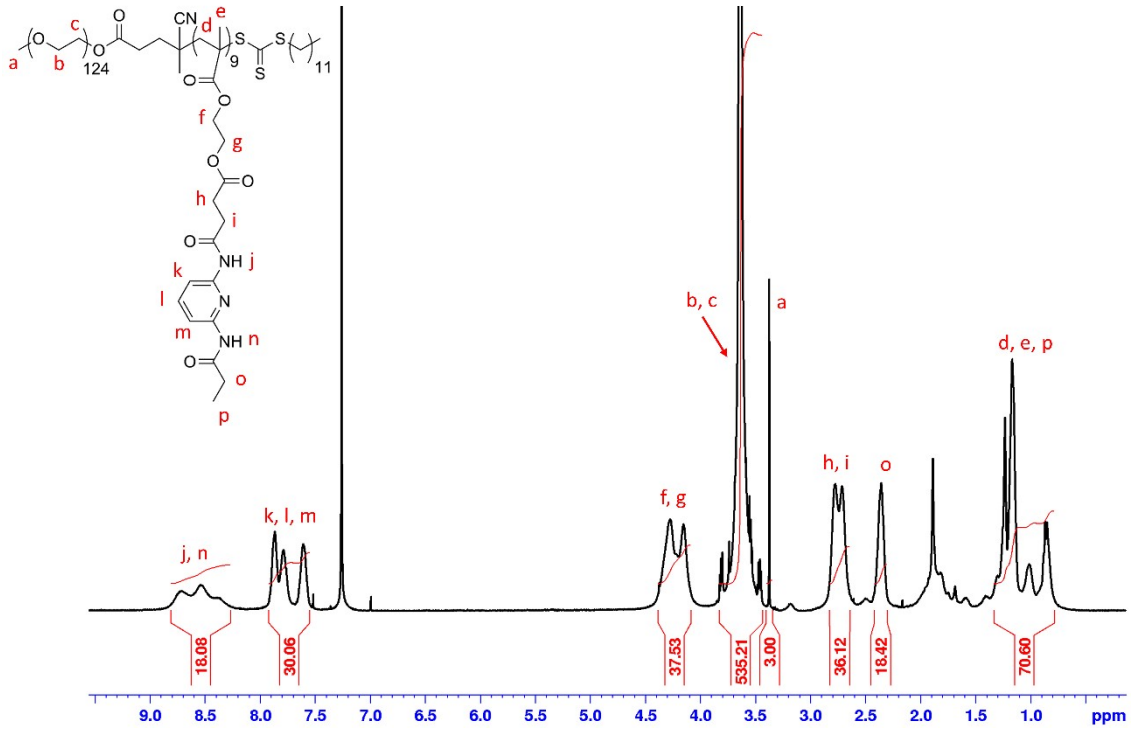

Fig. S3. ^{1}H NMR spectrum of **PEG$_{124}$-*b*-PDAP$_9$** ($CDCl_3$, 400 MHz) δ (ppm). In order to estimate PDAP degree of polymerization, the relative integration of proton signal at 3.37 ppm, corresponding to PEG block methyl terminal group (protons **a**) was compared to the one at 4.42-4.05 ppm, corresponding to DAP repeating unit (protons **f** and **g**).

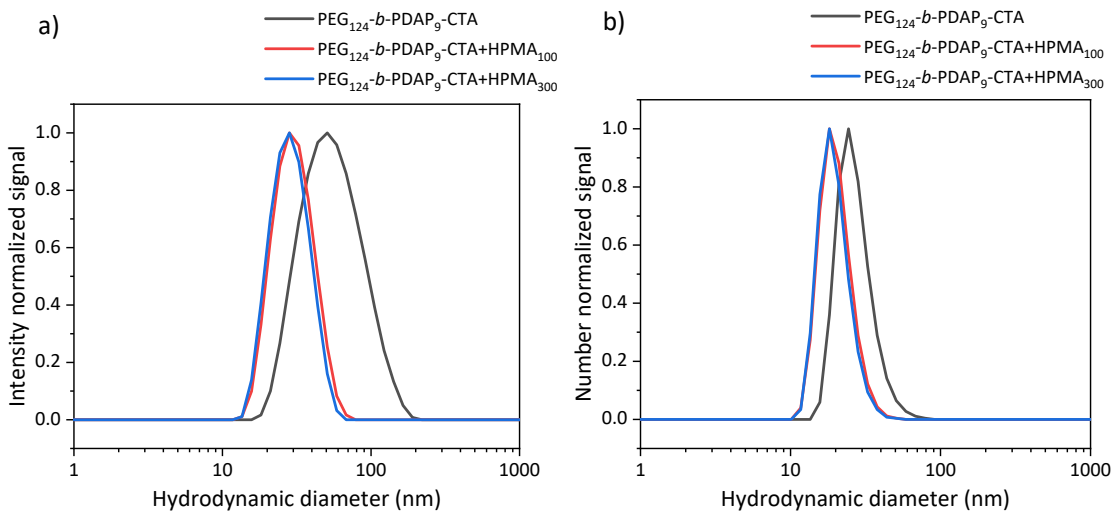

Fig. S4. (a) Intensity and (b) number particle size distributions recorded by DLS measurements of **PEG_{124}-*b*-$PDAP_9$-CTA, PEG_{124}-*b*-$PDAP_9$-CTA + $HPMA_{100}$** and **PEG_{124}-*b*-$PDAP_9$-CTA + $HPMA_{300}$** at polymerization temperature (50°C).

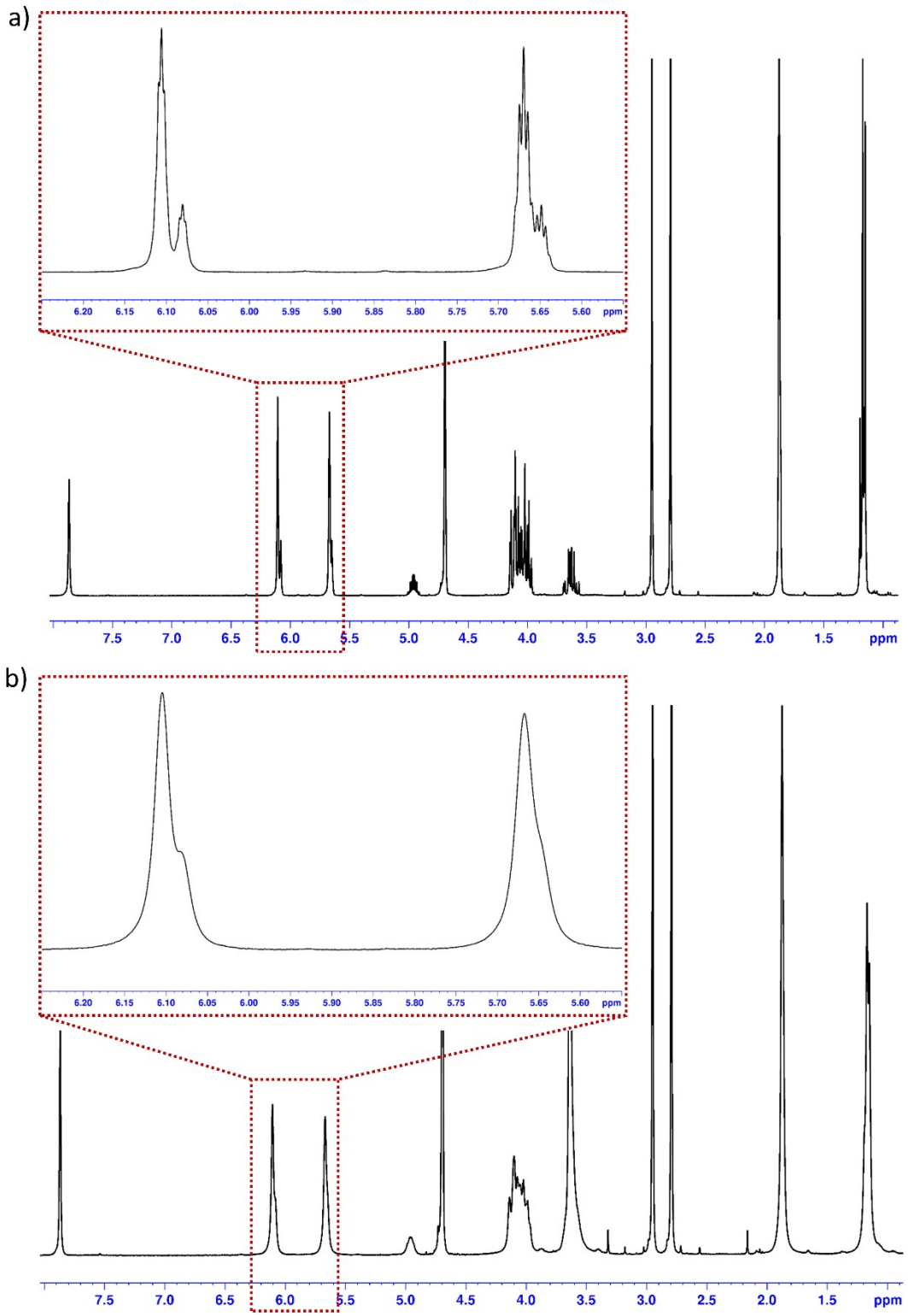

Fig. S5. ^{1}H NMR spectra (D_2O, 300 MHz) δ (ppm) recorded for (a) HPMA monomer (13 mg) dissolved in D_2O (0.7 mL), using DMF (5 µL) as internal standard and (b) a mixture of HPMA monomer (13 mg) and **PEG_{124}-*b*-$PDAP_9$-CTA** dissolved in D_2O (0.7 mL), using DMF (5 µL) as internal standard. Peak attenuation is observed for the HPMA vinyl signals in the presence of **PEG_{124}-*b*-$PDAP_9$-CTA** (compare insets) that HPMA preferentially is placed within **PEG_{124}-*b*-$PDAP_9$-CTA** self-assemblies rather than remaining in the aqueous phase.

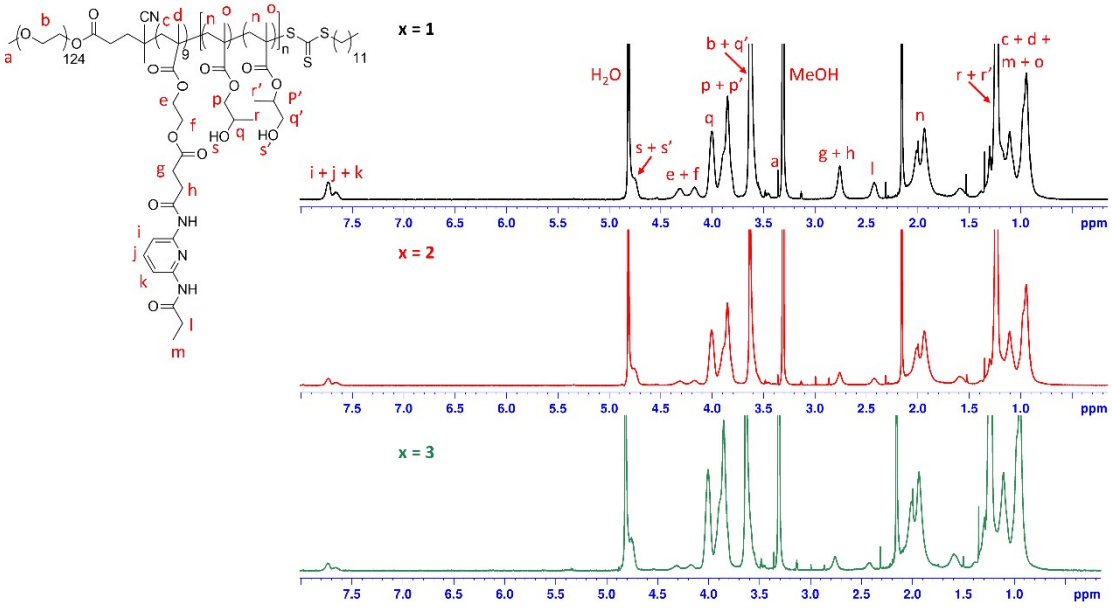

Fig. S6. Representative ^{1}H-NMR spectra of **PEG$_{124}$-*b*-PDAP$_9$-*b*-PHPMA$_n$** BCs formed at c=25 (CD_3OD, 400 MHz) δ (ppm).

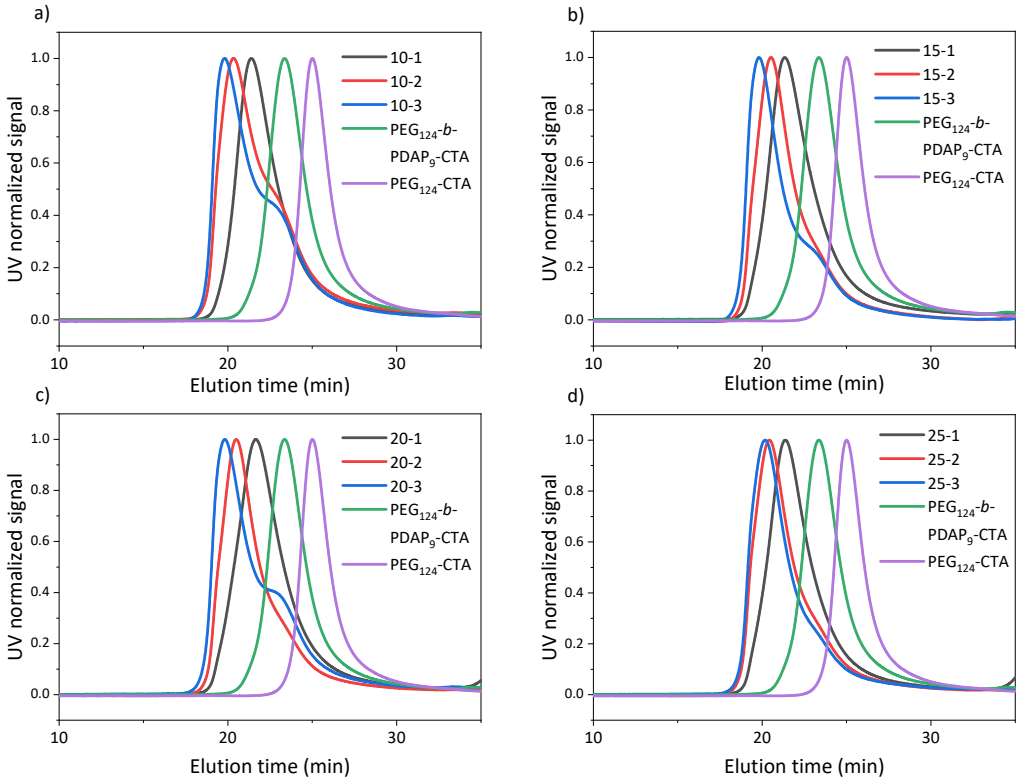

Fig. S7. GPC chromatograms recorded using a PDA detector at 290 nm, employing DMF (LiBr 50 mM) as eluent, of **PEG$_{124}$-*b*-PDAP$_9$-*b*-PHPMA$_n$** block copolymers polymerized at (a) 10, (b) 15, (c) 20 and (d) 25 g of polymer/100 mL of water.

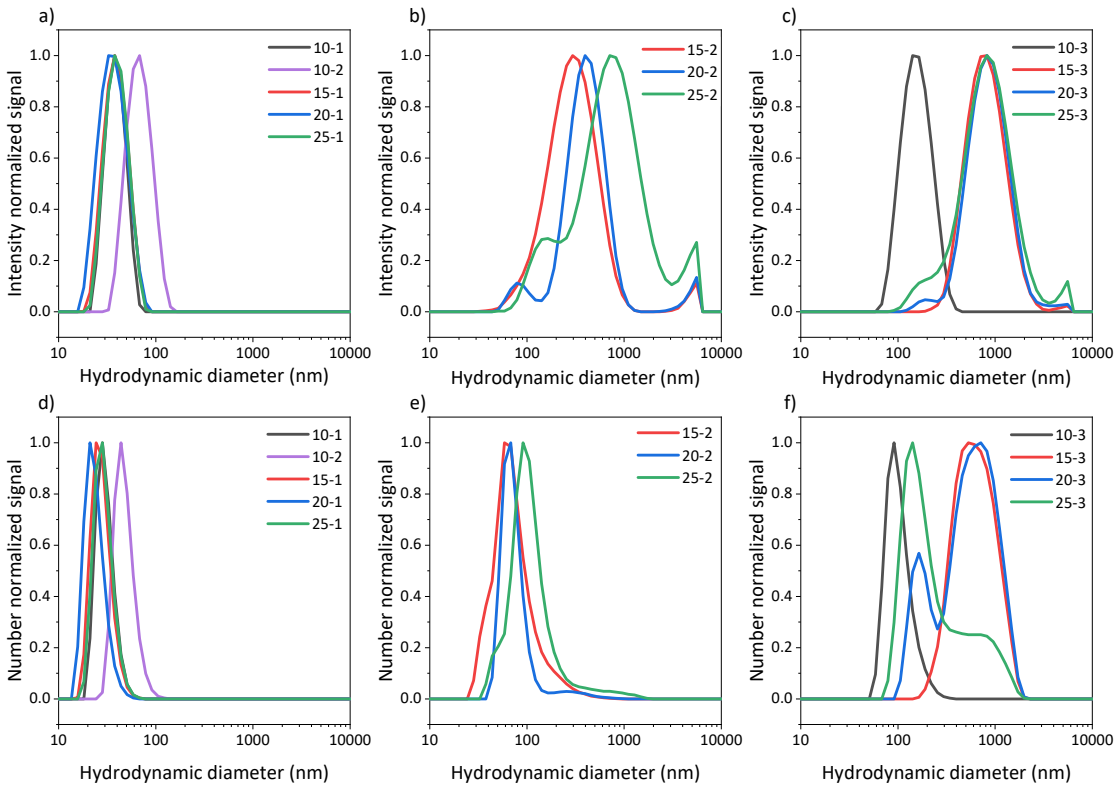

Fig. S8. First row: Intensity particle size distributions recorded by DLS of **PEG_{124}-*b*-$PDAP_9$-*b*-$PHPMA_n$** self-assemblies dispersions: (a) spherical micelles, (b) worms and (c) unilamellar and oligolamellar vesicles. Second row: Number particle size distributions recorded by DLS of **PEG_{124}-*b*-$PDAP_9$-*b*-$PHPMA_n$** self-assemblies dispersions: (a) spherical micelles, (b) worms and (c) unilamellar and oligolamellar vesicles.

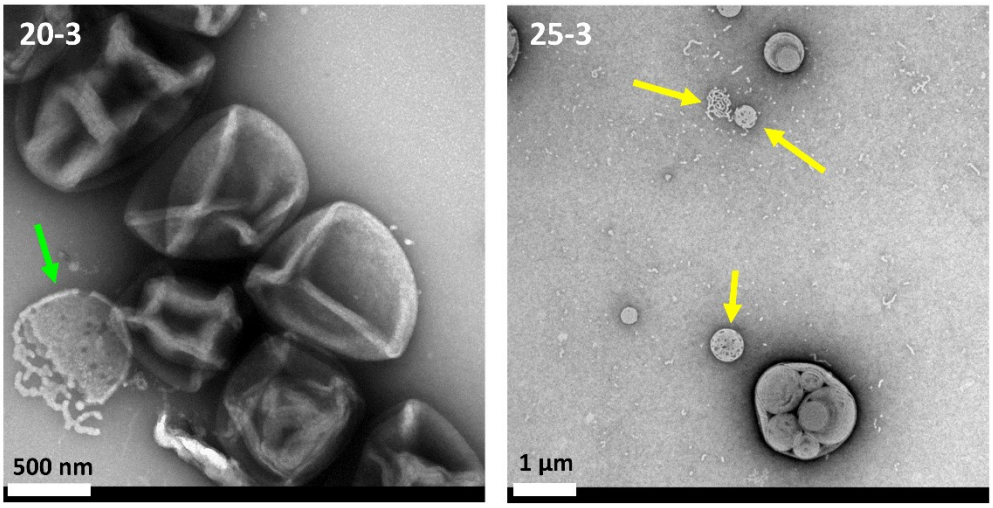

Fig. S9. TEM images of **PEG_{124}-*b*-$PDAP_9$-*b*-$PHPMA_n$** dispersions of series x=3 that show transition morphologies such as wormballs and coalesced wormballs (yellow arrows) and jellyfish (green arrow).

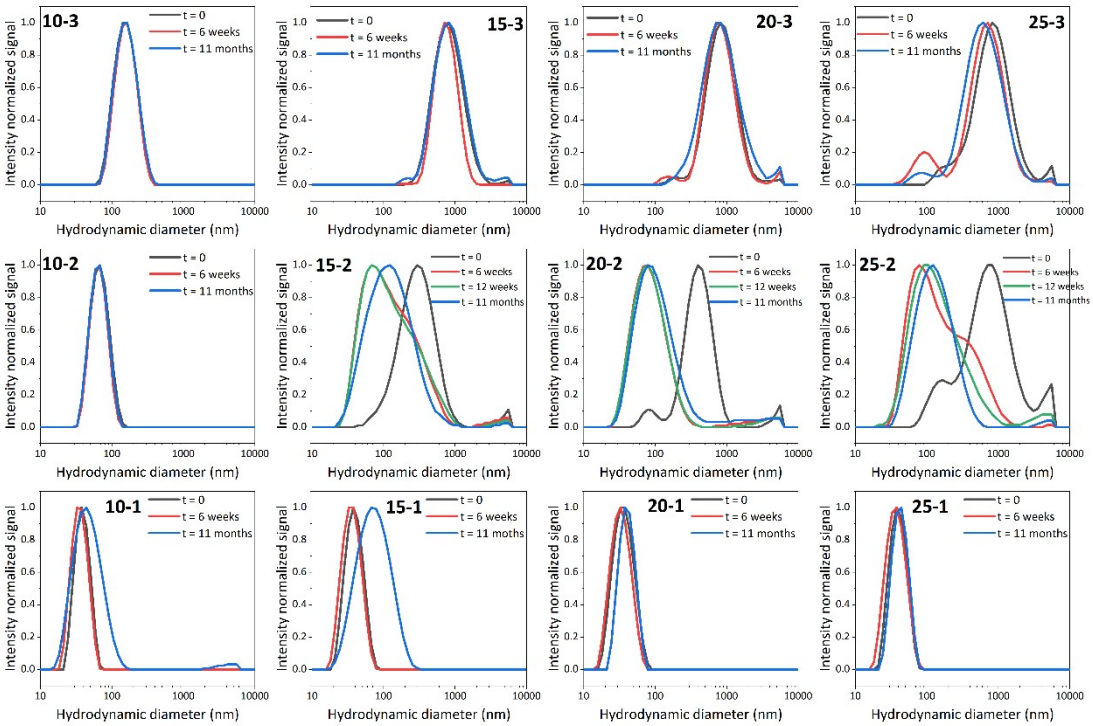

Fig. S10. Evolution of average size distributions over time for **PEG$_{124}$-*b*-PDAP$_9$-*b*-PHPMA$_n$** samples registered by DLS.

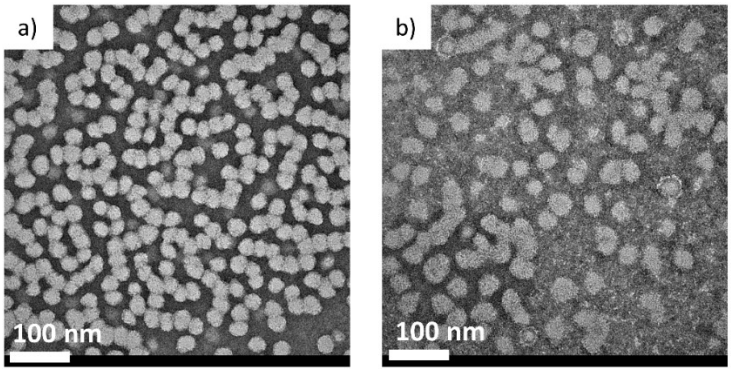

Fig. S11. TEM images of dispersions (a) 10-1 and (b) 15-1, taken 11 months after the aqueous seeded RAFT polymerization.

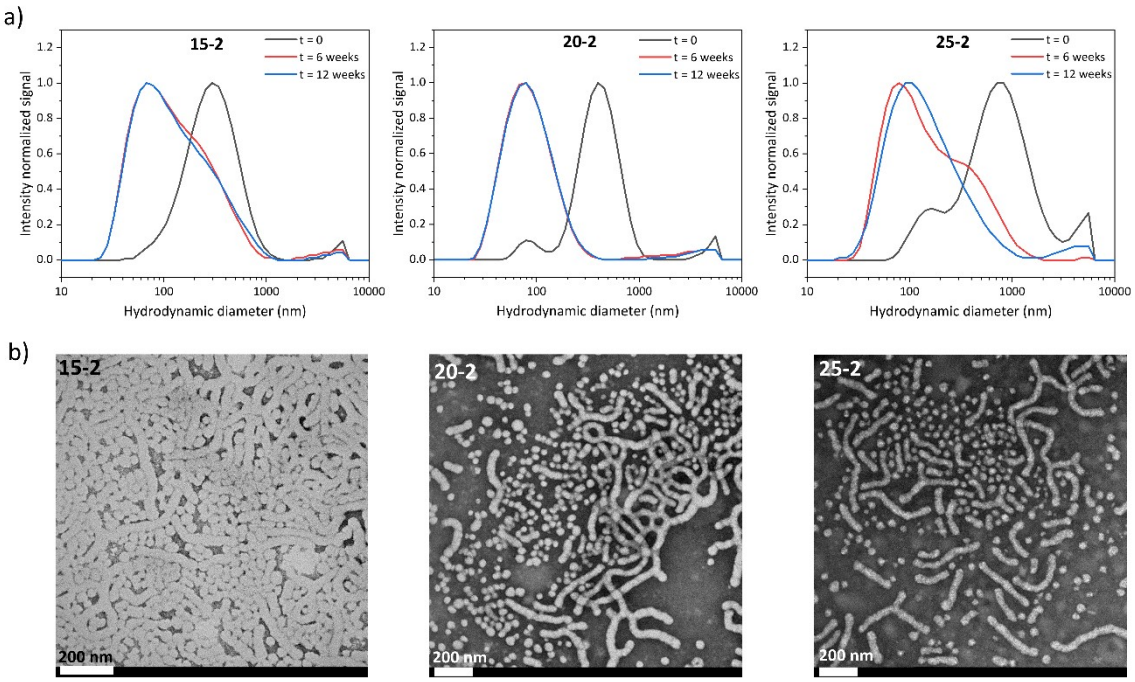

Fig. S12. (a) DLS measurements over time of worm-like dispersions. (b) TEM images of worm-like dispersions 12 weeks after polymerization.

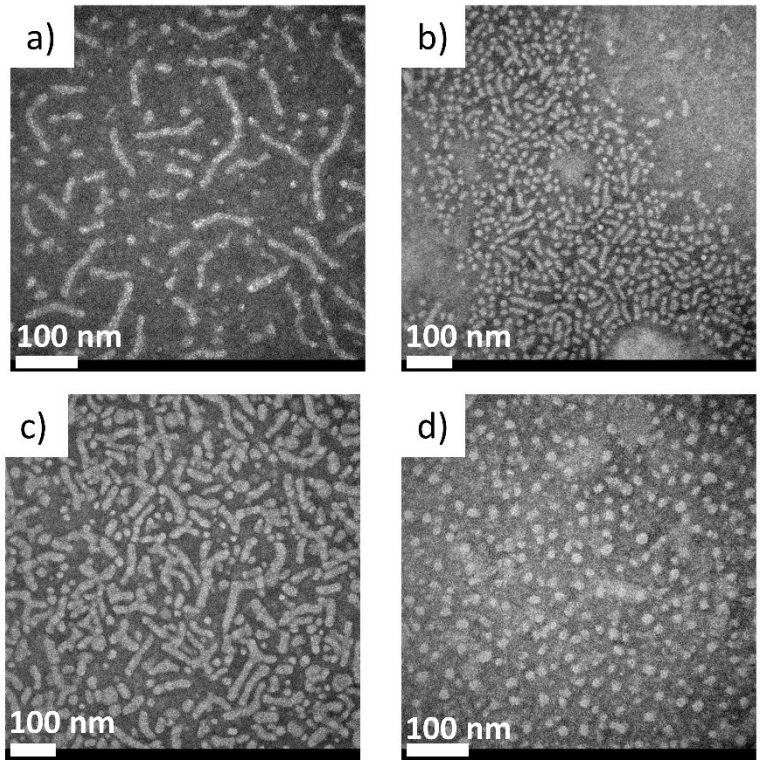

Fig. S13. TEM images of (a) **PEG_{124}-*b*-$PDAP_9$-CTA**, (b) **PEG_{124}-*b*-$PDAP_9$-CTA + $HPMA_{100}$**, (c) **PEG_{124}-*b*-$PDAP_9$-CTA + T_4** and (d) **PEG_{124}-*b*-$PDAP_9$-CTA + T_4 + $HPMA_{100}$** self-assemblies in water.

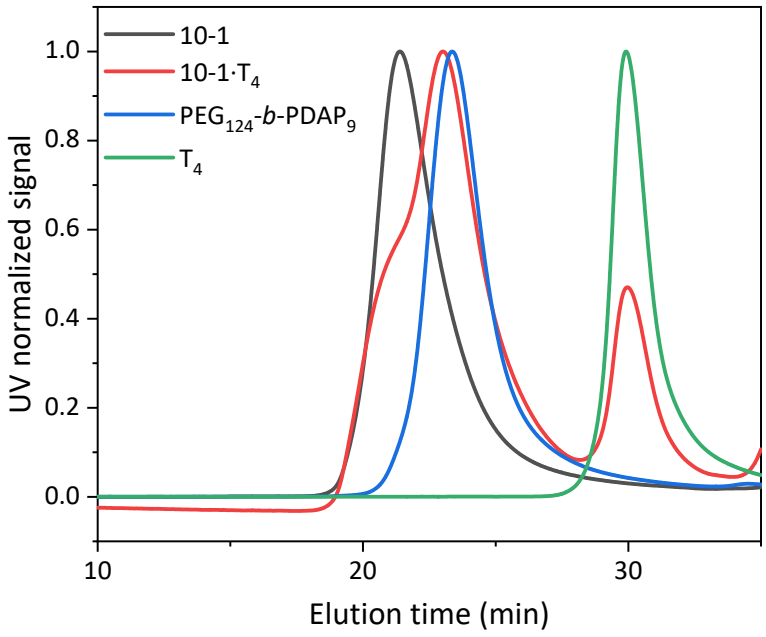

Fig. S14. GPC chromatograms using DMF as eluent of **10-1·T_4**, **10-1**, **PEG_{124}-*b*-$PDAP_9$-CTA** and **T_4**.

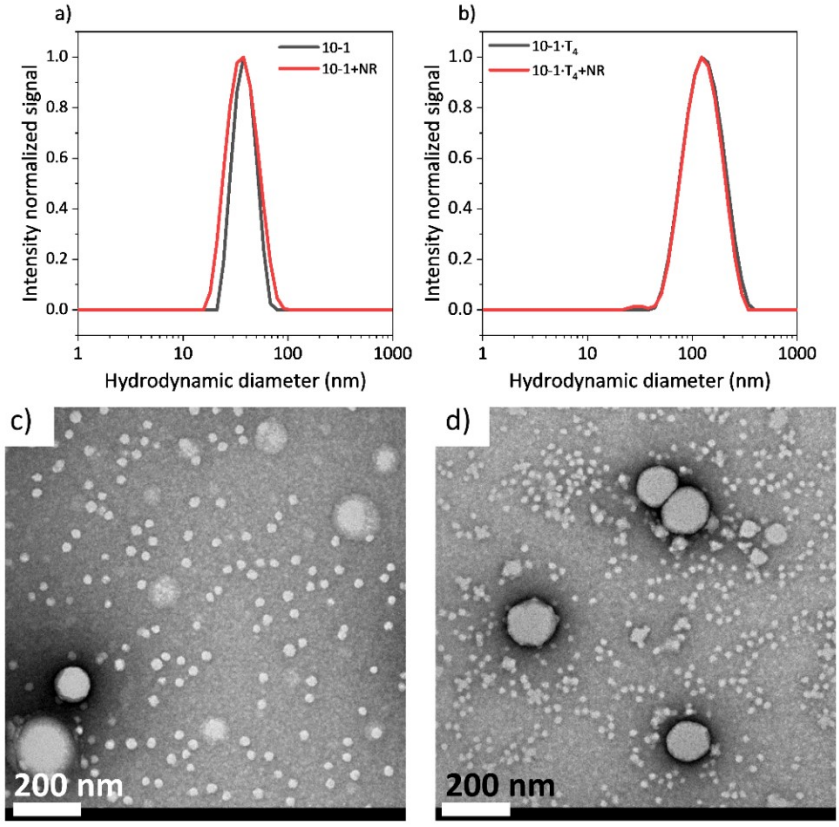

Fig. S15. DLS measurements of NR loaded and non-loading (a) **10-1** and (b) **10-1·T_4** polymeric aggregates. TEM images of (c) **10-1+NR** and (d) **10-1·T_4+NR** polymeric self-assemblies.

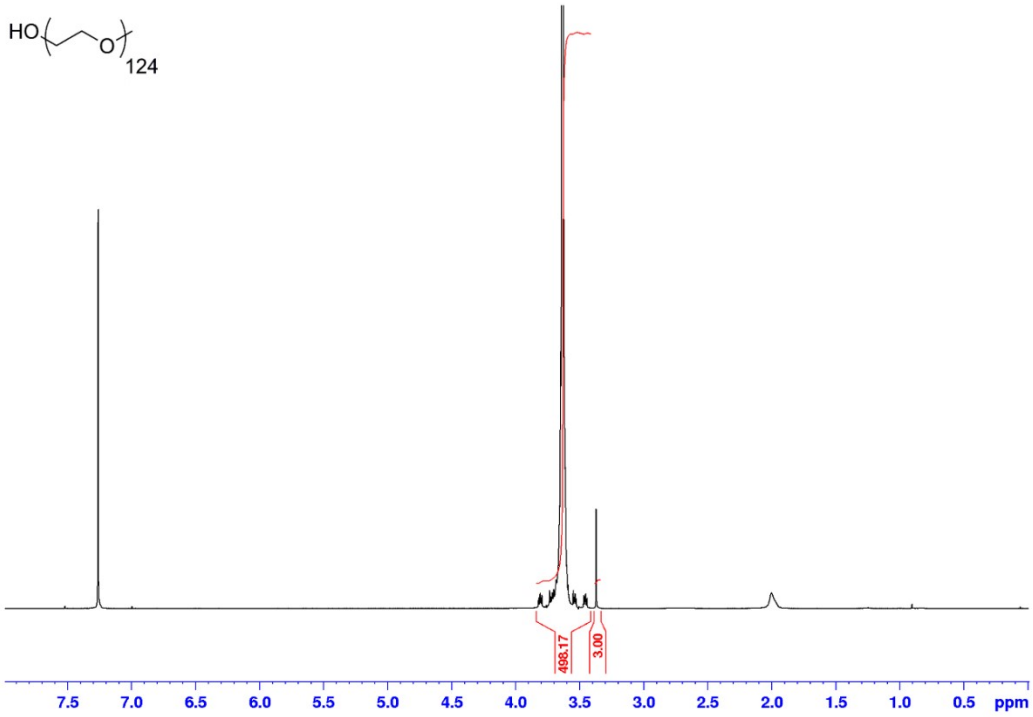

Fig. S16. ^{1}H-NMR spectrum of **PEG_{124}-OH** ($CDCl_3$, 400 MHz) δ (ppm).

Table S1. Characterization data obtained from **PEG_{124}-OH**, **PEG_{124}-CTA**, **PEG_{124}-*b*-$PDAP_9$-CTA**, **PEG_{124}-*b*-$PDAP_9$-*b*-$PHPMA_n$** and **PEG_{124}-*b*-$PDAP_9$-*b*-$PHPMA_n$·T_4** polymers.

Sample	Conversion	PHPMA degree of polymerization[a]	Average M_n	Hydrophilic/ hydrophobic ratio[d]	M_n (GPC)[e]	$Đ$[e]
PEG_{124}-OH	--	--	5450[b]	--	--	--
PEG_{124}-CTA	--	--	5840[b]	93/7	22605	1.07
PEG_{124}-*b*-$PDAP_9$-CTA	93%	--	9440[b]	58/42	32910	1.18
10-1	>99%	115	26000[c]	21/79	53165	1.32
10-2	99%	214	40300[c]	13/87	64840	1.42
10-3	98%	338	58200[c]	9/91	72810	1.42
15-1	>99%	105	24600[c]	22/78	55180	1.31
15-2	>99%	219	41000[c]	13/87	73790	1.31
15-3	>99%	336	57900[c]	9/91	83385	1.38
20-1	>99%	111	25500[c]	21/79	50900	1.34
20-2	>99%	217	40700[c]	13/87	66990	1.41
20-3	>99%	326	56500[c]	10/90	71045	1.45
25-1	>99%	104	24500[c]	22/78	54630	1.34
25-2	>99%	213	40200[c]	14/86	71995	1.35
25-3	>99%	314	54700[c]	10/90	78510	1.35
10-1·T_4	98%	111	25400[c]	21/79	45390	1.31

[a]Estimated taking into account polymerization conversion. [b]Average number molar mass (M_n) determined by ^{1}H-NMR spectroscopy. [c]Average number molar mass (M_n) calculated taking into account the **PEG_{124}-*b*-$PDAP_9$-CTA** average M_n estimated by ^{1}H-NMR and the PHPMA degree of polymerization. [d]Hydrophobic/hydrophilic weight percentage ratio estimated from M_n, considering the PEG block as the hydrophilic part and the rest of the polymer as the hydrophobic part. [e]Relative average number molar mass M_n, and dispersity ($Đ$) determined by GPC using DMF with 50 mM LiBr (0.5 mL min^{-1}) and PS standards calibration.