Supporting Information

Biodegradable Multiblock Poly[*N*-(2-Hydroxypropyl)methacrylamide] via Reversible Addition-Fragmentation Chain Transfer Polymerization and Click Chemistry

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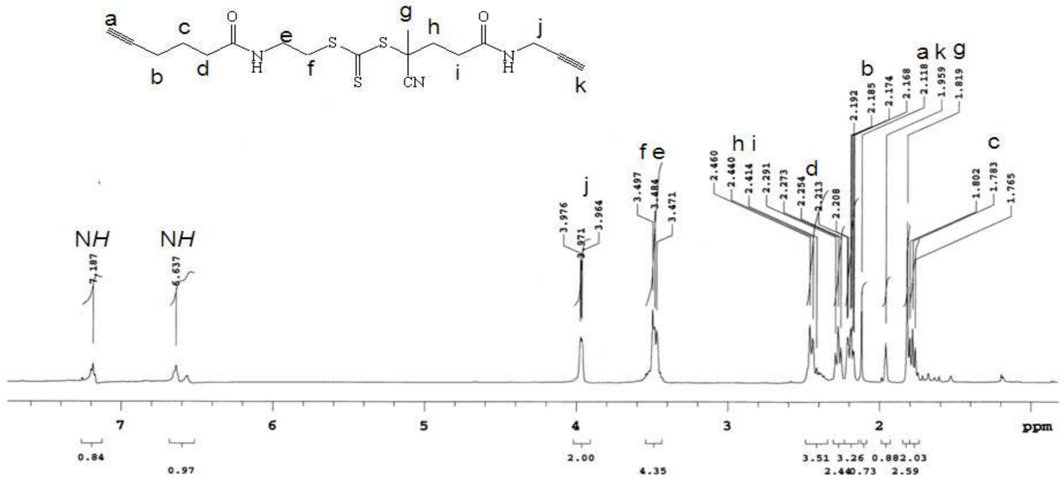

Figure S1. ^{1}H NMR spectrum of S-2-cyano-5-oxo-5-(prop-2-ynylamino)pentan-2-yl S'-(*N*-hex-5-ynoyl)aminoethyl trithiocarbonate (dialkyne-CTA) (recorded in $CDCl_3$).

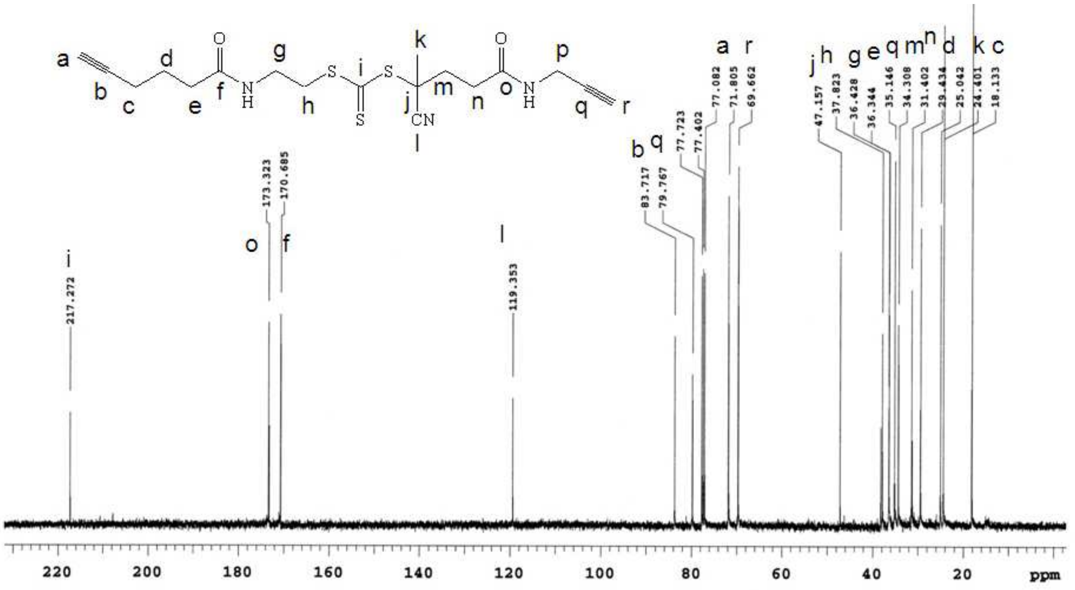

Figure S2. ^{13}C NMR spectrum of *S*-2-cyano-5-oxo-5-(prop-2-ynylamino)pentan-2-yl S'-(*N*-hex-5-ynoyl)aminoethyl trithiocarbonate (dialkyne-CTA) (recorded in $CDCl_3$).

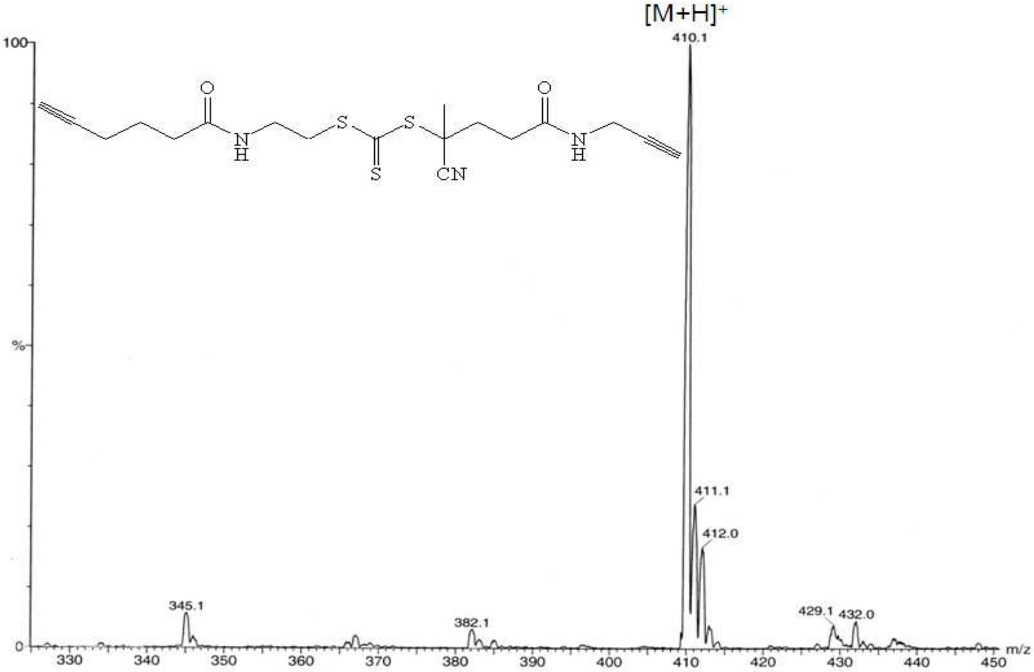

Figure S3. ESI mass spectrum of S-2-cyano-5-oxo-5-(prop-2-ynylamino)pentan-2-yl S'-(*N*-hex-5-ynoyl)aminoethyl trithiocarbonate (dialkyne-CTA) . The mass of CTA calculated: 409.1 Da; observed: 410.1 Da $[M + H]^+$.

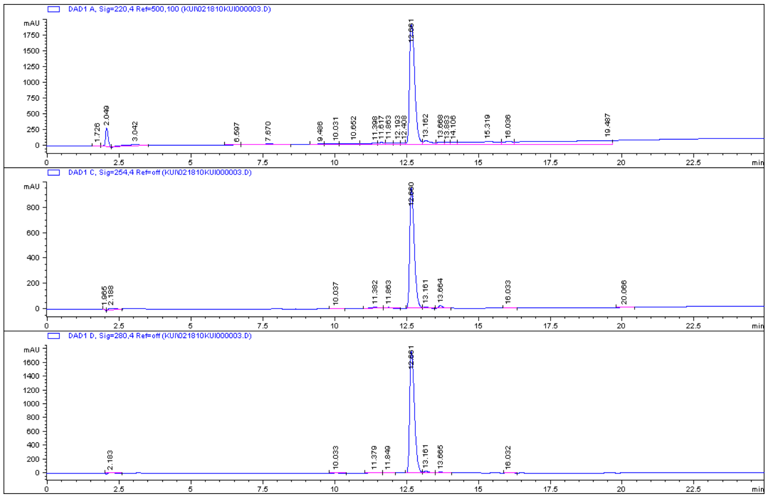

Figure S4. HPLC profile of dialkyne-CTA.

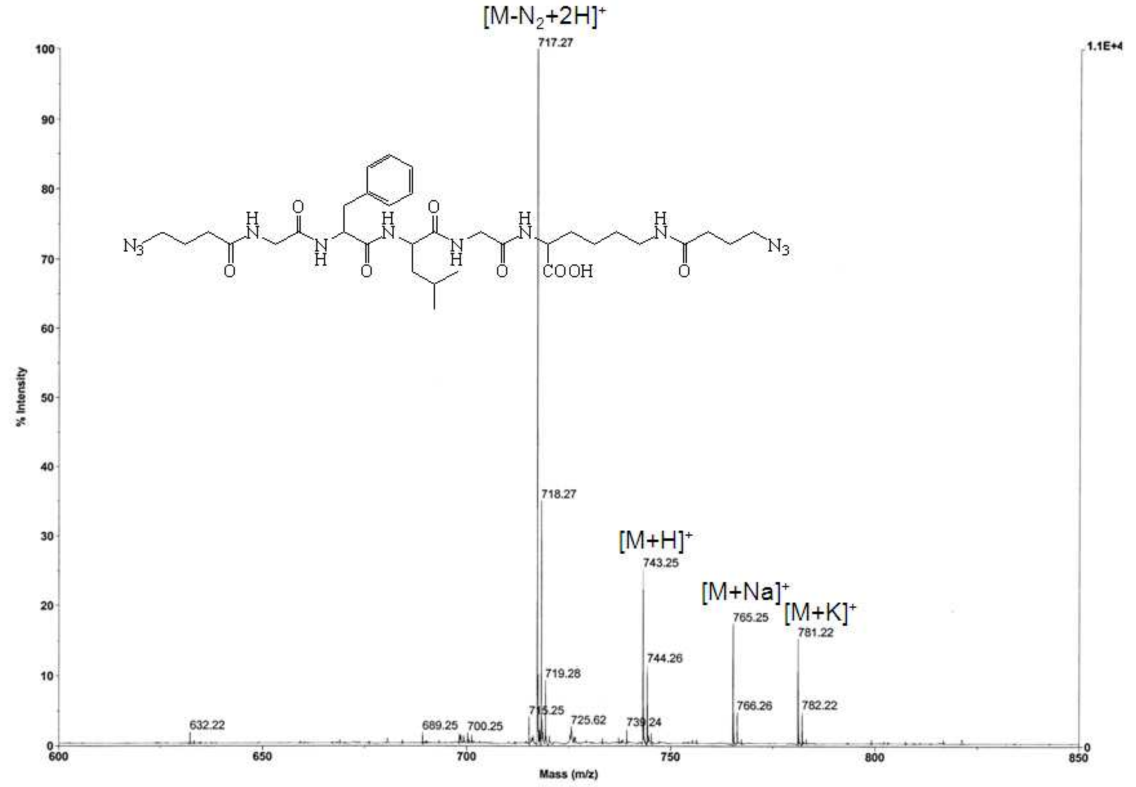

Figure S5. MALDI TOF mass spectrum of the α,ω-diazide GFLG. The mass of peptide was calculated to be 742.39 Da; experimental peaks were observed at 717.27, 743.25, 765.25 and 781.22 Da.

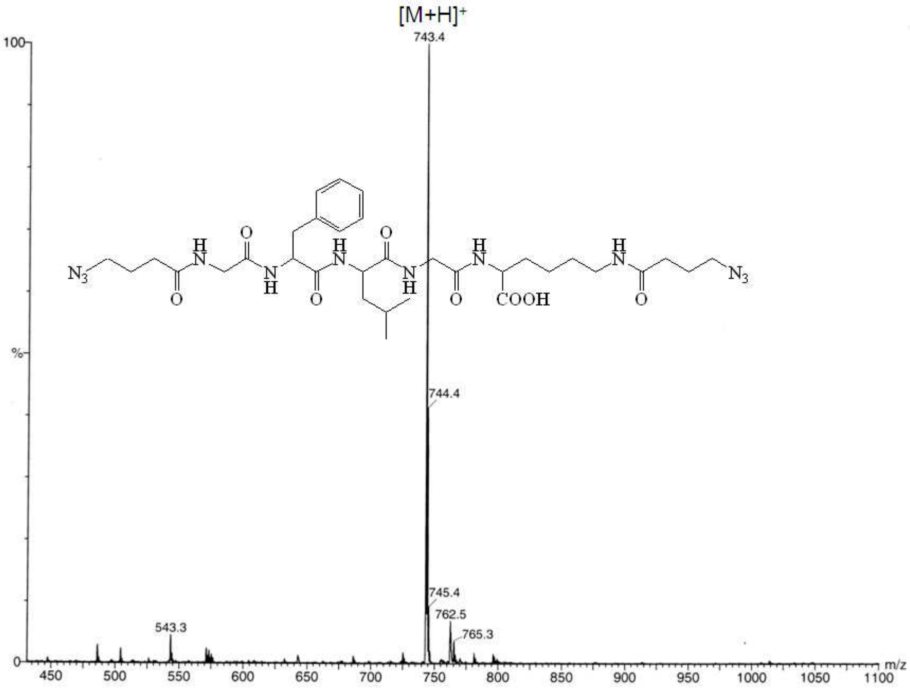

Figure S6. ESI mass spectrum of α,ω-diazide GFLG, The mass of peptide: calculated 742.4 Da; observed 743.4 Da

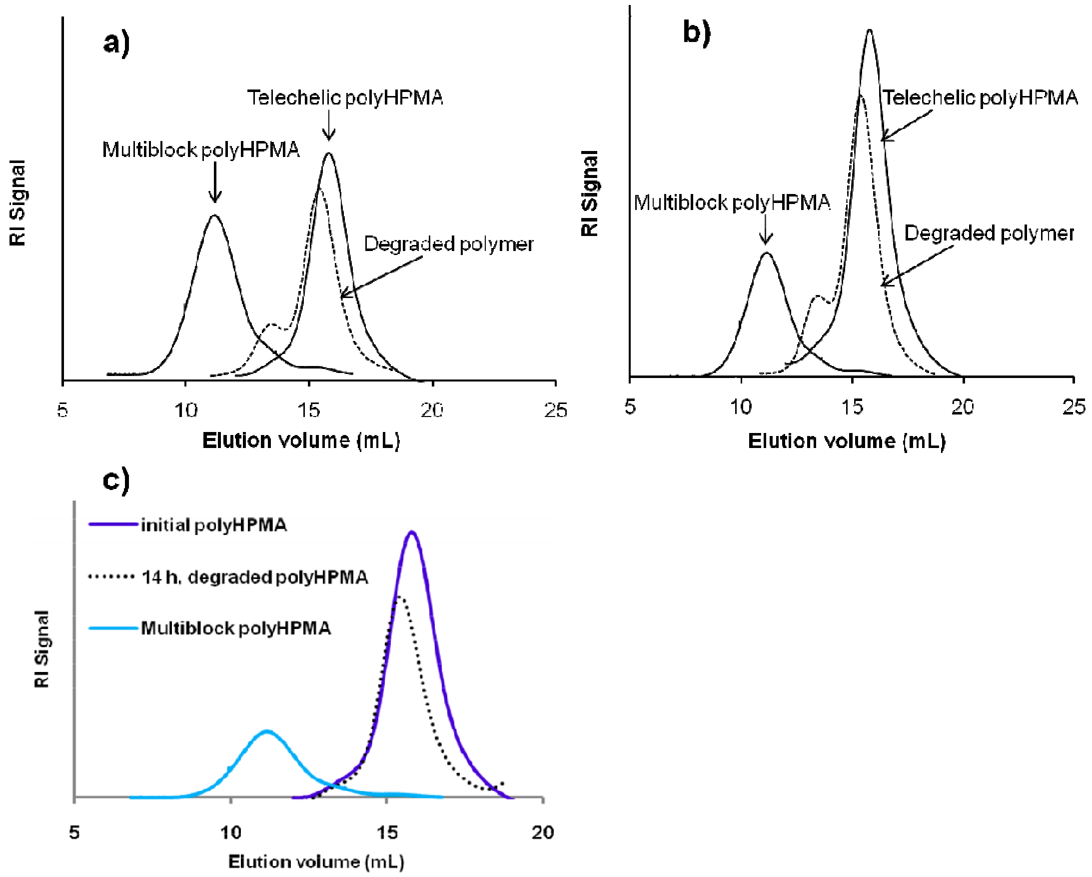

Figure S7. Degradation of multiblock polyHPMA fraction (Mn = 182 kDa, PDI = 1.07) after 14 h of incubation with **a**) Papain; degraded polymer (Mn = 49 kDa, PDI = 1.04); **b**) Cathepsin B; degraded polymer (Mn = 49 kDa, PDI = 1.04); and **c**) Papain; degraded polymer (Mn = 48 kDa, PDI = 1.03), papain was added twice – at the start of the experiment and at 8 h. The multiblock polyHPMA was prepared from an initial telechelic α,ω-dialkyne polyHPMA (Mn = 43 kDa, PDI = 1.05). Mn and PDI were measured using size-exclusion chromatography (SEC) on an AKTA FPLC system using a Superose 6 HR/10/30 column with PBS (pH 7.3) as mobile phase.

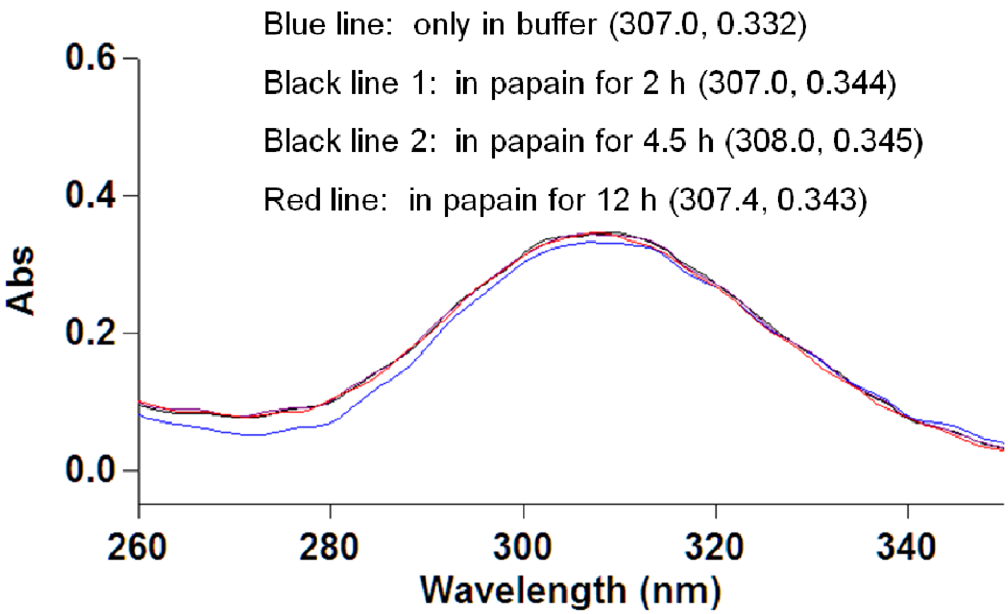

Figure S8. UV-vis spectra of α,ω-dialkyne polyHPMA incubated in buffer containing no papain (blue line) and in the solution of papain at conditions identical with those used for multiblock polymer degradation (the two black lines and the red line).

Table S1. HPMA RAFT polymerization in water mediated by α,ω-dialkyne CTA[a]

Entry	Time h	Conv. [b] %	Mn, calc. kDa	Mn, SEC kDa [c]	PDI[c]
1	0.5	10.4	4.1	3.4[d]	1.06
2	1.0	12.4	5.2	6.9	1.05
3	1.5	19.9	8.3	10.4	1.06
4	2.0	25.6	10.7	12.5	1.07
5	2.5	29.1	12.1	13.2	1.07
6	3.0	35.5	14.8	14.9	1.07
7	3.5	40.6	16.9	16.4	1.08
8	4.0	44.1	18.4	19.7	1.05
9	4.5	50.1	20.9	22.2	1.04
10	5.0	53.0	22.1	23.4	1.07
11	5.5	59.2	24.7	25.9	1.05

[a] $[HPMA]_0$ = 1 M, $[HPMA]_0/[CTA]_0/[I]_0$ = 290/1/0.25. Polymerization was carried out at 60 °C with AIBN as the initiator.

[b] Monomer conversion determined by HPLC.

[c] Determined by FPLC using a Superose 12 HR/10/30 column with PBS (pH 7.3) as mobile phase.