Supporting Information

Synthesis of poly(*tert*-butyl acrylate) dibromide (Br-P*t*BA-Br). P*t*BA dibromide was synthesized by atom transfer radical polymerization (ATRP) according to a previously reported method.[1] *Tert*-butyl acrylate (*t*-BA) was passed through a column of basic alumina to remove inhibitors prior to use. For the synthesis of PtBA with a molecular weight of 2,800 g/mol [as calculated by NMR (Br-P*t*BA_{22}-Br)], *t*-BA (70.22 mmol), CuBr (2.18 mmol), PMDETA (2.16 mmol), dimethyl 2,6-dibromoheptanedioate (4.37 mmol), and 4.5 mL anhydrous toluene were added to a 100 mL Schlenk flask. The dark green reaction mixture was degassed via three freeze-pump-thaw cycles. The flask was then backfilled with nitrogen, sealed, and stirred in an oil bath at 80 °C. Stirring was continued for 2 h. After cooling the flask, THF (~10 mL) was added to reduce the viscosity of the reaction mixture. The diluted solution was filtered through a column of basic alumina to remove copper and washed with additional THF. The yellow filtrate was concentrated by rotary evaporation, precipitated twice into a mixture of 50/50 methanol/water in an ice bath, and dried under vacuum. The viscous, pale yellow polymer was collected in 46% yield and analyzed by ^{1}H NMR and GPC. ^{1}H NMR ($CDCl_3$, δ): 4.12 (m, 1H, $CH_2C\boldsymbol{H}$-Br), 3.65 (s, 3H, $OC\boldsymbol{H_3}$), 2.26 (m, 11H, $CH_2C\boldsymbol{H}CO$), 1.87, 1.64-1.56 (m, 22H, $C\boldsymbol{H_2}CHCO$), 1.46 (s, 99H, $C(C\boldsymbol{H_3})_3$). M_n (by NMR) = 2,800 g/mol. GPC (based on calibration with polystyrene standards): M_n = 2,570 g/mol, M_w = 3,090 g/mol, PDI = 1.2.

A similar procedure was followed for the synthesis of PtBA with a molecular weight of 8,000 g/mol by NMR (Br-P*t*BA_{63}-Br), adjusting the monomer to initiator ratio (156.4 mmol *t*-BA, 2.19 mmol dimethyl 2,6-dibromoheptanedioate) to achieve the desired molecular weight. ^{1}H NMR ($CDCl_3$, δ): 4.10 (m, 1H, $CH_2C\boldsymbol{H}$-Br), 3.60 (s, 3H, $OC\boldsymbol{H_3}$), 2.19 (m, 32H, $CH_2C\boldsymbol{H}CO$), 1.87, 1.64

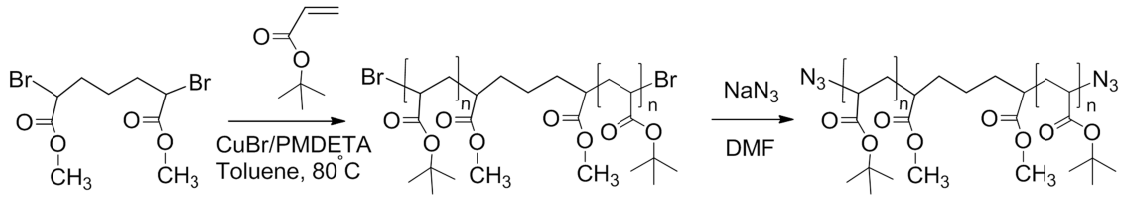
(m, 66H, C***H₂***CHCO), 1.46 (s, 298H, C(C***H₃***)$_3$). GPC (based on calibration with polystyrene standards): M_n = 8,290 g/mol, M_w = 10,740 g/mol, PDI = 1.3.

Synthesis of poly(*tert*-butyl acrylate) diazide (N_3-P*t*BA-N_3). In a typical procedure, Br-P*t*BA-Br (2.98 mmol) was added under nitrogen to an oven-dried, round bottom flask and dissolved in 6 mL anhydrous DMF. Sodium azide (1.1 equiv. to Br) was added to the flask and the reaction mixture was stirred at 70 °C under nitrogen for 24 h. The product was precipitated twice into cold 50/50 methanol/water and dried under vacuum to obtain a pale yellow solid in 74% yield. ^{1}H NMR ($CDCl_3$, δ) of N_3-P*t*BA_{22}-N_3: 3.74 (m, 1H, CH_2CH-N_3), 3.61 (s, 3H, OC***H₃***), 2.24 (m, 11H, CH_2CH), 1.81, 1.67-1.50 (m, 22H, C***H₂***CH), 1.44 (s, 99H, C(C***H₃***)$_3$).

Synthesis of X(VPGVG)$_2$X peptide (XVG2X). Peptides were synthesized by standard Fmoc protocols on a PS3 (Protein Technologies, Inc., Tucson, AZ) solid phase peptide synthesizer. The peptide X(VPGVG)$_2$X (where V = valine, P = proline, G = glycine, and X = propargylglycine) was synthesized on Rink Amide MBHA resin (Novabiochem, EMD Chemicals, San Diego, CA) which results in an amide group at the C-terminus, and the N-terminus was capped by reaction with acetic anhydride. After the synthesis was complete, the resin was washed with DCM, collected by vacuum filtration, and stirred in a mixture of 95/2.5/2.5 TFA/water/triisopropylsilane for 4-6 h at room temperature to simultaneously cleave the peptide from the resin and to remove side-chain protecting groups. After the resin was removed, the filtrate was precipitated twice into cold ether, and the white precipitate was collected by centrifugation. The pellet was dissolved in water and lyophilized to obtain a fluffy, white solid in 49% yield. The mass of X(VPGVG)$_2$X was confirmed via ESI mass spectrometry: (*m*/*z*) 1090.5 [$(M + Na)^+$, calculated 1091.0]. ^{1}H NMR (D_2O) δ (ppm): 7.89-8.31 (m, N***H***CO), 3.95-4.50 (m, 12H, NH-C***H***-CO), 3.63 (m, 4H, proline NHC$H_2CH_2CH_2$), 2.73 (m, 4H,

C*H*$_2$C≡CH), 2.45 (m, 2H, CH$_2$C≡C*H*), 1.93-2.25 (m, 12H, valine CH(CH$_3$)$_2$ and proline NHCH$_2$CH$_2$CH$_2$), 0.96 (m, 24H, valine CH(CH$_3$)$_2$).

Estimation of the radius of gyration for PAA and [PAA$_{22}$-VG2]$_n$ multiblock copolymers. The radius of gyration (R_g) for the PAA segments was estimated to be 0.66 nm for PAA$_{22}$ with M_n = 1,600 g/mol and 1.2 nm for PAA$_{63}$ with M_n = 4,500 g/mol, based on reported values for poly(methacrylic acid) (PMA) in acidic aqueous solution,[2] and scaled as $R_g \sim N^{\upsilon}$, where N is the degree of polymerization and υ=3/5 considering water as a good solvent. The peptide was calculated from the jointed chain model to have a R_g of 0.52 nm (by assuming a mostly random coil structure with individual segments having a 0.37 nm length per residue).[3] Considering these dimensions and the average of 3-6 blocks per chain indicated by the GPC results, the [PAA$_{22}$-VG2]$_n$ individual, unassembled (soluble) multiblock polymer chains should have a radius of gyration of approximately 1.8-3.5 nm, and [PAA$_{63}$-VG2]$_n$ chains should have a radius of gyration approximately 2.9-5.2 nm.



Scheme S1. Synthesis of azide-functionalized P*t*BA.

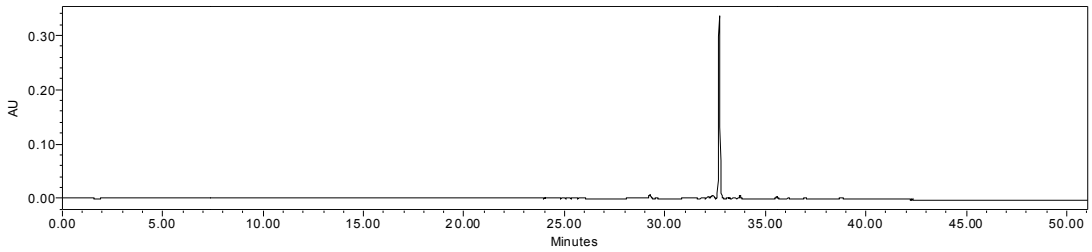


Figure S1. HPLC of VG2 peptide (Waters Symmetry C18 column, 3.5 µm, 4.6 x 75 mm); 5-55% acetonitrile gradient in water with 0.1% TFA; UV detector at 214 nm.

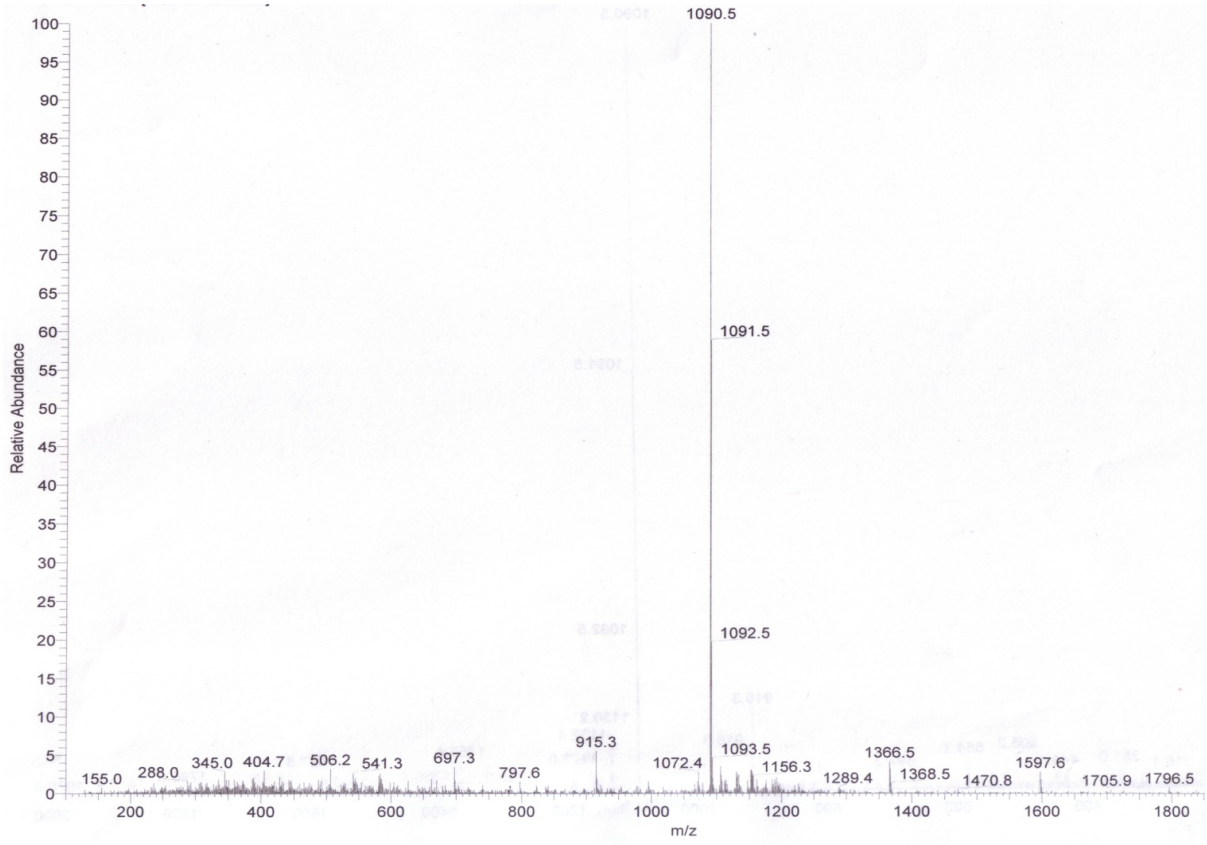


Figure S2. ESI-MS (positive ion mode) of VG2.

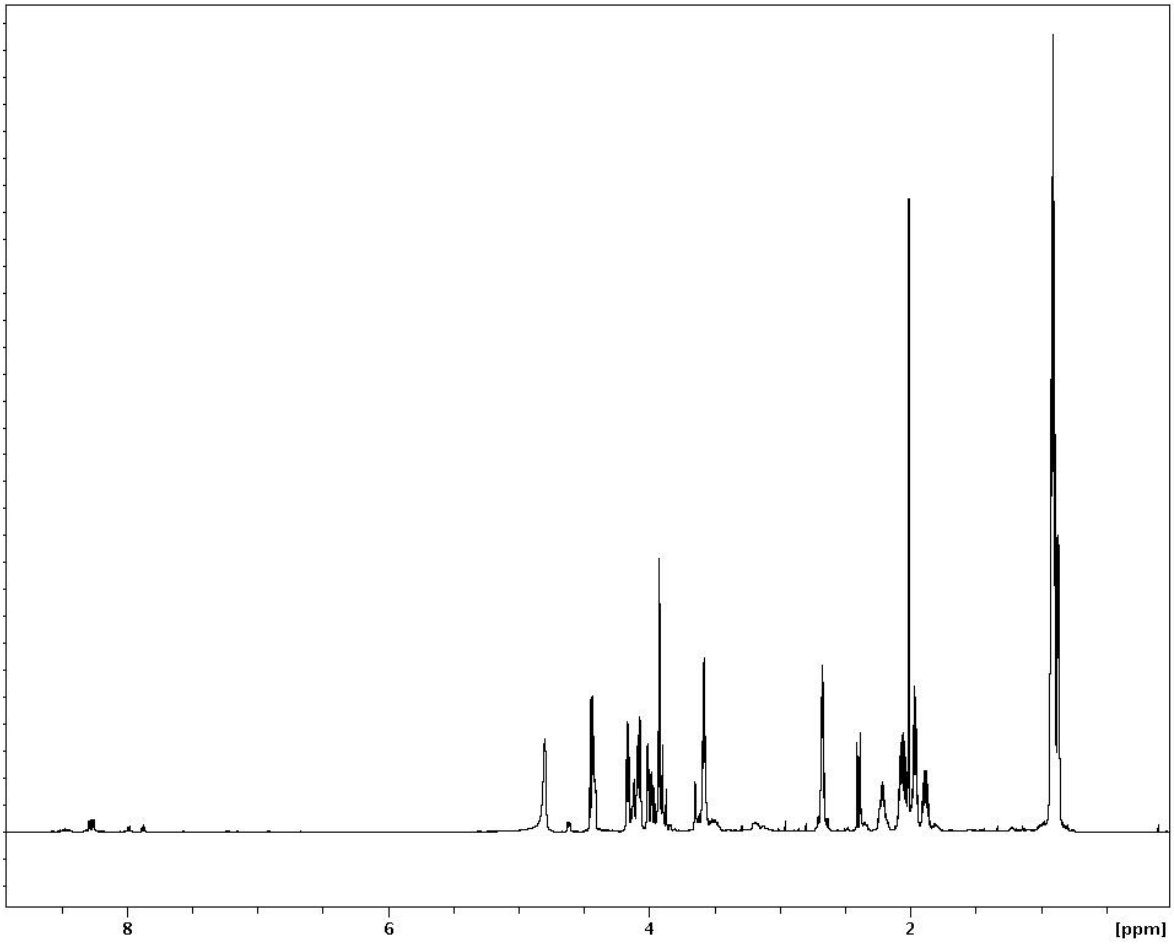


Figure S3. ^{1}H NMR of VG2 in D_2O.

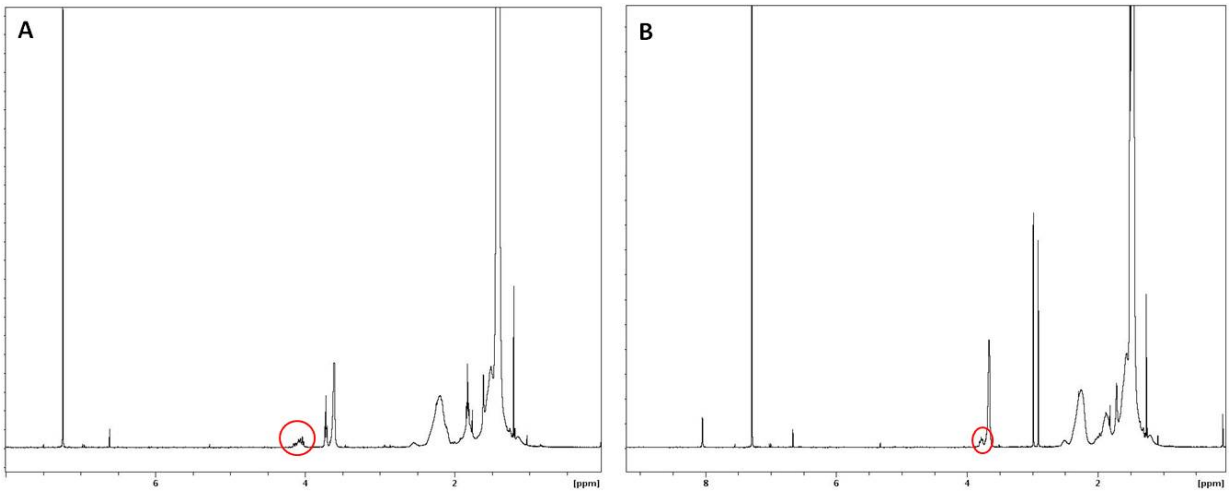


Figure S4. ^{1}H NMR characterization of P*t*BA precursors. A: ^{1}H NMR spectrum of Br-P*t*BA$_{22}$-Br in $CDCl_3$; B: ^{1}H NMR spectrum of N_3-P*t*BA$_{22}$-N_3 in $CDCl_3$. Peaks from the end group, C***H***C(O)O(CH_3), in both polymers are circled.

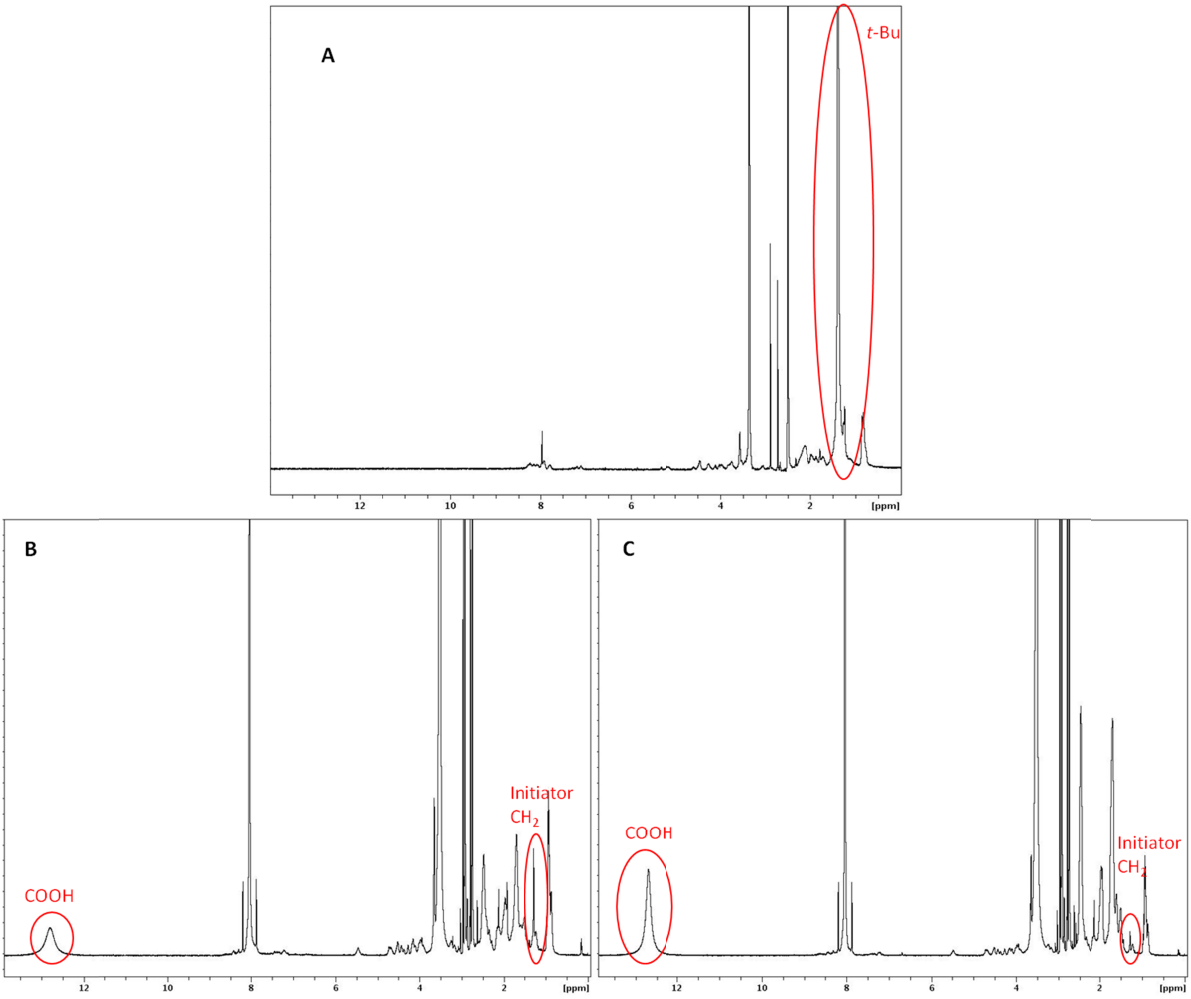


Figure S5. NMR characterization of $[PtBA\text{-}VG2]_n$ and $[PAA\text{-}VG2]_n$ multiblock copolymers. A: ^1H NMR spectrum of $[PtBA_{22}\text{-}VG2]_n$ in DMSO-d_6; B: ^1H NMR spectrum of $[PAA_{22}\text{-}VG2]_n$ in DMF-d_7; C: ^1H NMR spectrum of $[PAA_{63}\text{-}VG2]_n$ in DMF-d_7.

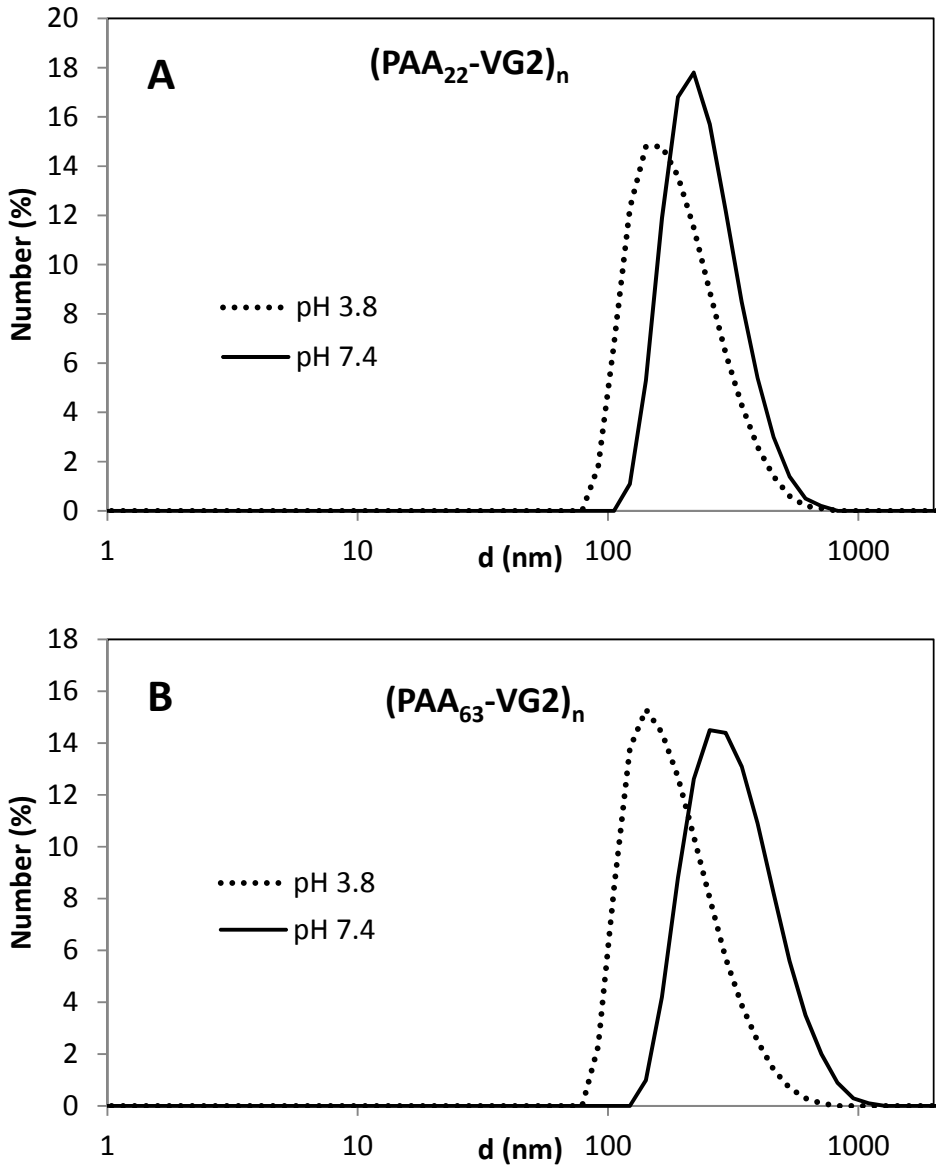


Figure S6. DLS size distribution by number for $[PAA_{22}\text{-}VG2]_n$ (A) and $[PAA_{63}\text{-}VG2]_n$ (B) at pH 3.8 (dashed line) and pH 7.4 (solid line).

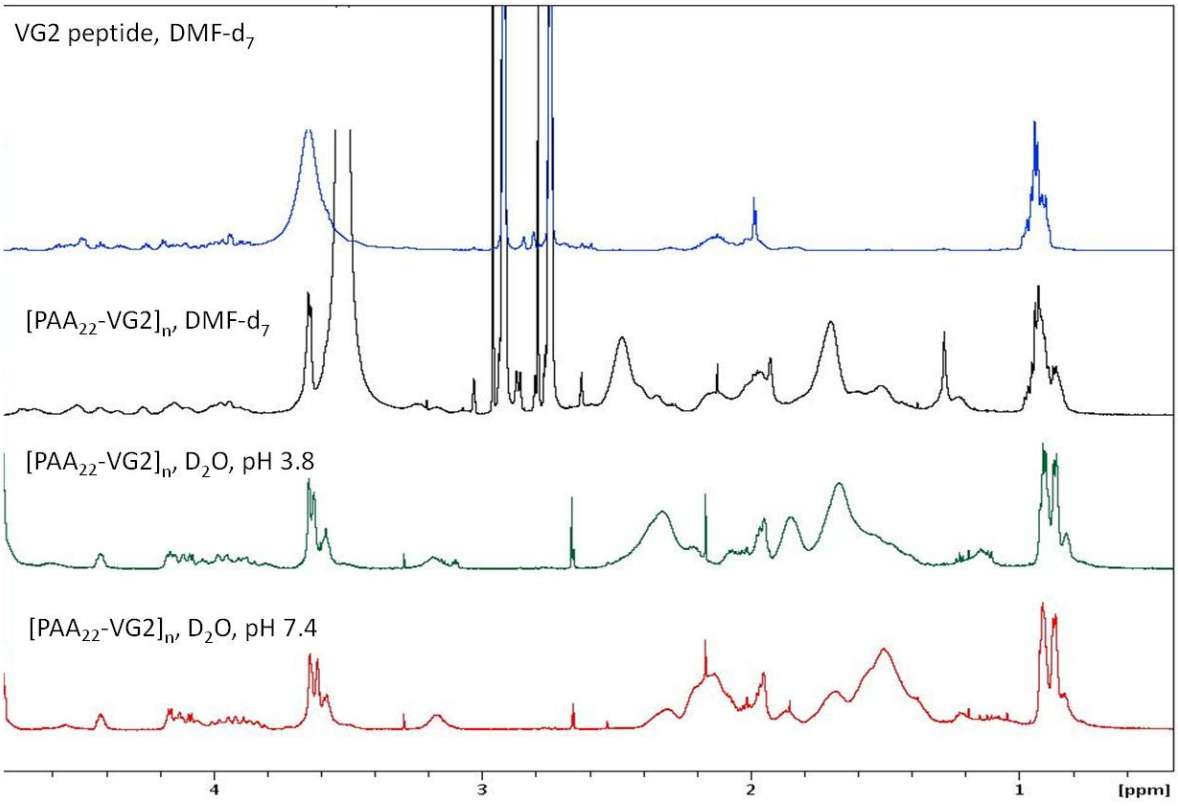


Figure S7. ^{1}H NMR of VG2 peptide in DMF-d_7 (blue), $[PAA_{22}\text{-}VG2]_n$ in DMF-d_7 (black), $[PAA_{22}\text{-}VG2]_n$ in D_2O at pH 3.8 (green), and $[PAA_{22}\text{-}VG2]_n$ in D_2O at pH 7.4 (red).

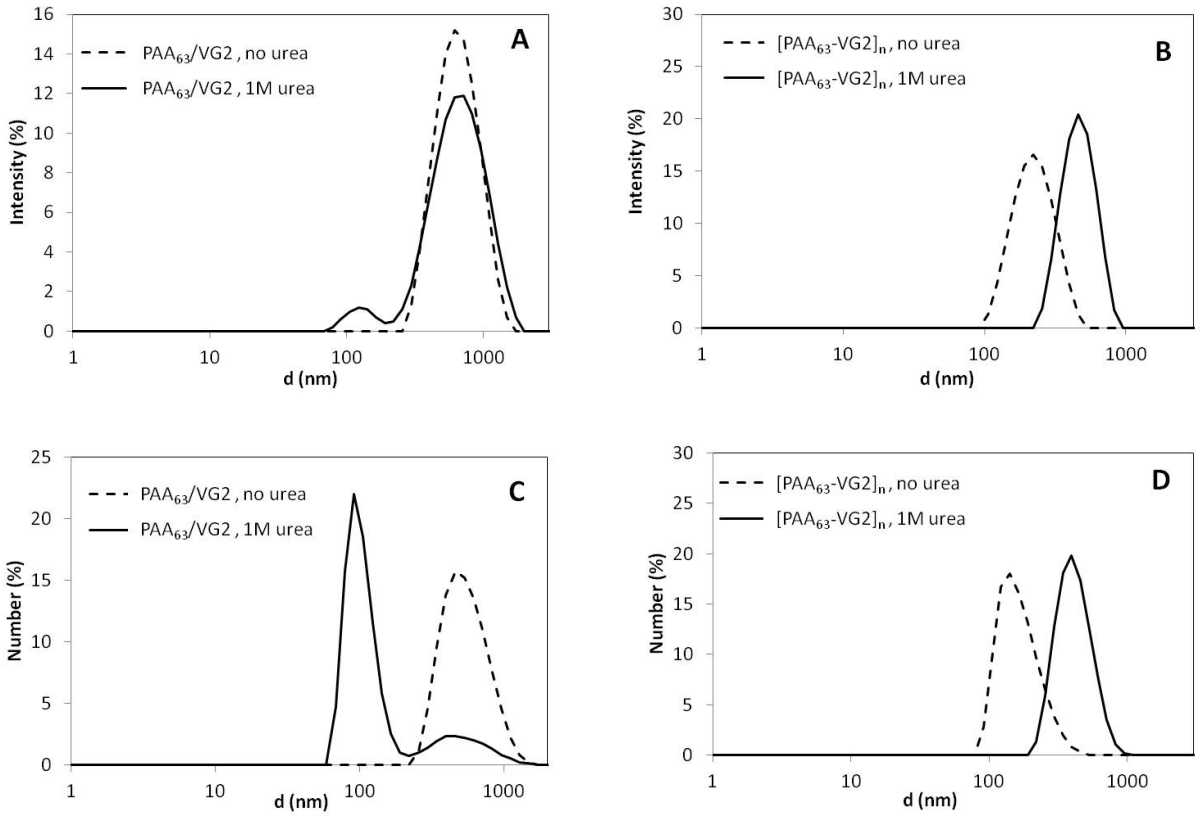


Figure S8. DLS size distributions of PAA_{63}/VG2 physical mixtures (A: intensity, C: number) and $[PAA_{63}\text{-VG2}]_n$ multiblock copolymers (B: intensity, D: number) in water without urea (dashed lines) and with urea during particle formation (solid lines).

References

1. P. L. Golas, N. V. Tsarevsky, B. S. Sumerlin and K. Matyjaszewski, *Macromolecules*, 2006, **39**, 6451-6457.
2. Y. Muroga, T. Yoshida and S. Kawaguchi, *Biophysical Chemistry*, 1999, **81**, 45-57.
3. K. E. Gebhardt, S. Ahn, G. Venkatachalam and D. A. Savin, *Journal of Colloid and Interface Science*, 2008, **317**, 70-76.