Electronic Supplementary Material (ESI) for Biomaterials Science.

Supporting Information

Interplay Between the Linker and Polymer Molecular Weight of a Self-Assembling Prodrug on the Pharmacokinetics and Therapeutic Efficacy

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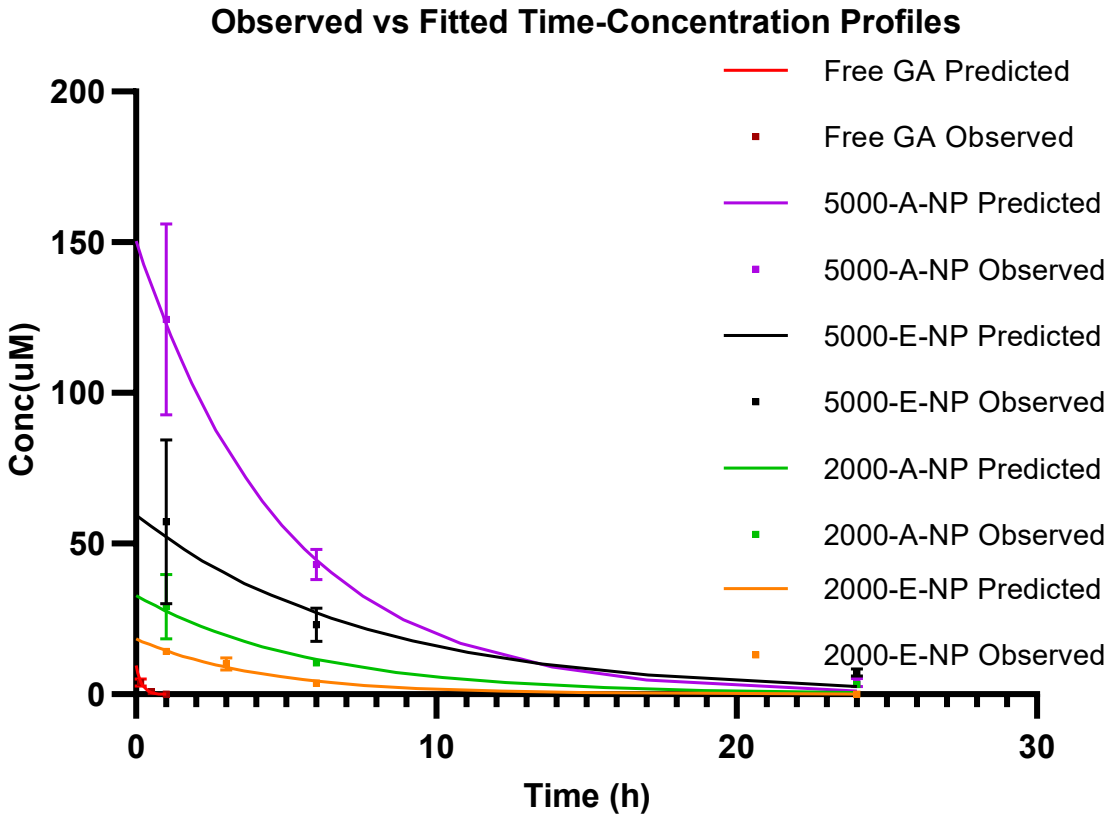

Figure S1. Fitted vs observed concentration-time profile. Smoothed line indicates the predicted population average concentration-time profile using non-compartment IV bolus model. Squares with vertical error bars represents the observed concentrations at each time point from mice (n = 6-9).

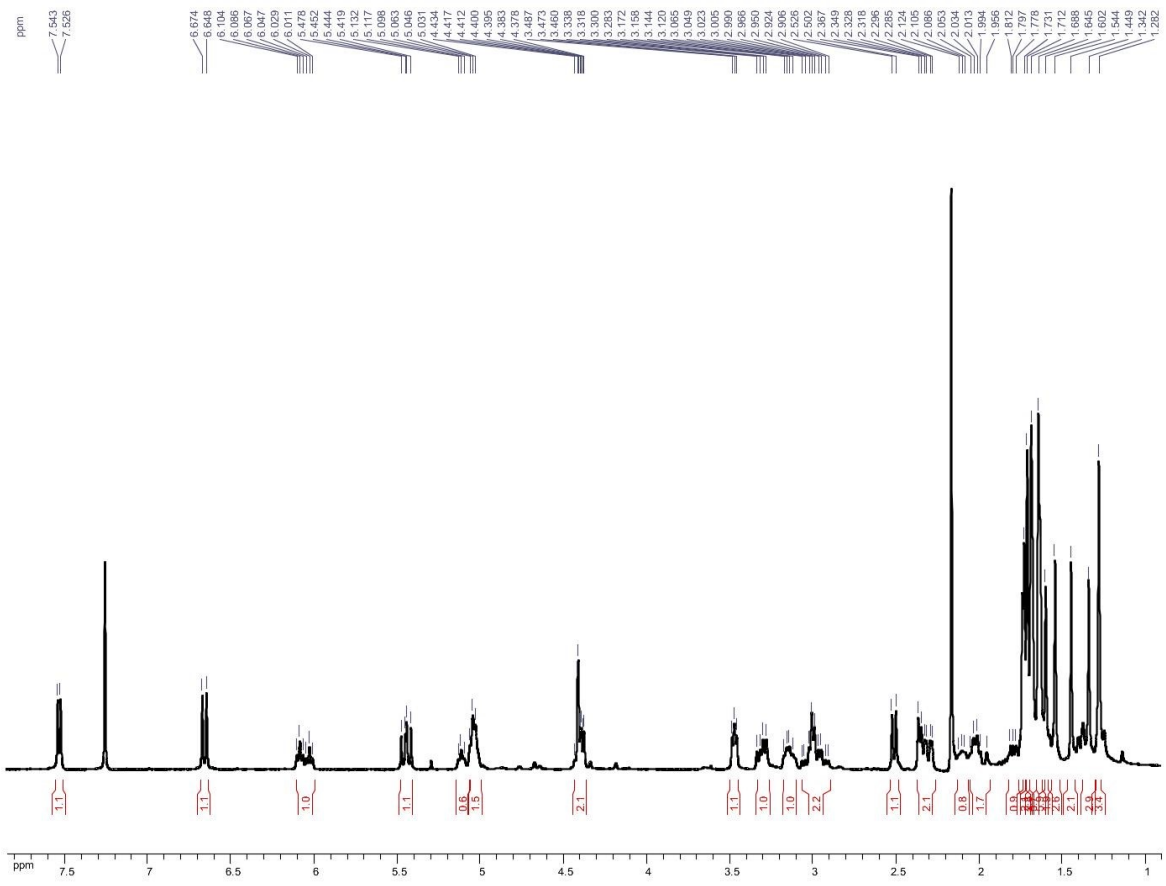

Figure S2. ^{1}H-NMR spectrum of GAyne-ester
^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 12.745-12.835 (d, 1H), 7.543-7.526 (d, 1H), 6.674-6.648 (d, 1H), 6.104-6.011 (m, 1H), 5.478-5.419 (m, 1H), 5.132-5.098 (m, 1H), 5.063-5.031 (m, 1H), 4.434-4.378 (m, 2H), 3.487-3.460 (m, 1H), 3.338-3.283 (m, 1H), 3.172-3.120 (m, 1H), 3.065-2.906 (m, 2H), 2.526-2.502 (d, 1H), 2.367-2.285 (m, 2H), 2.124-2.086 (m, 1H), 2.053-1.956 (m, 2H, 1.812-1.778 (t, 1H), 1.731 (s, 3H), 1.712 (s, 2H), 1.688 (s, 6H), 1.645 (s, 6H), 1.602 (s, 2H), 1.544 (s, 3H), 1.449 (s, 2H), 1.342 (s, 3H), 1.282 (s, 3H)

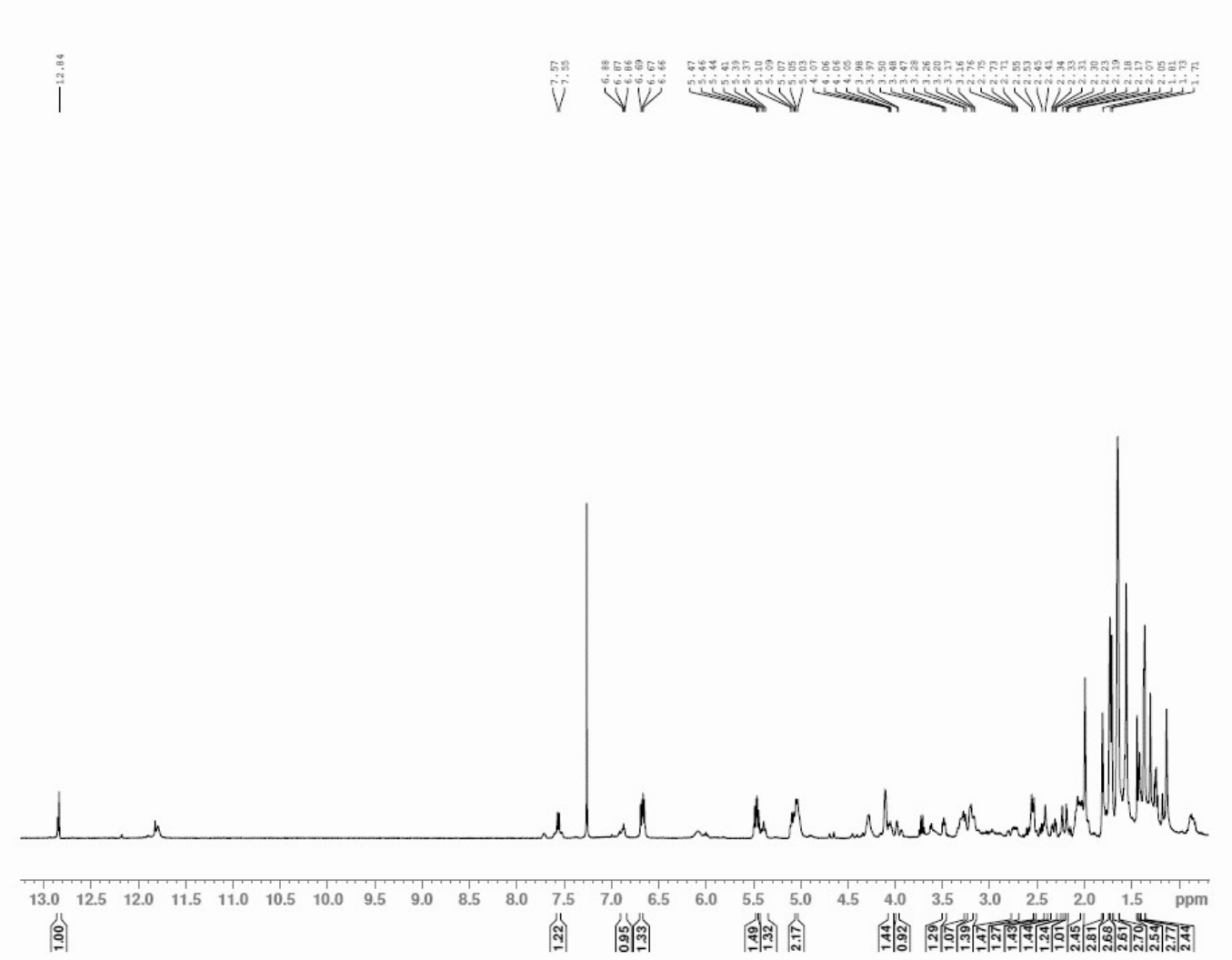

Figure S3. ^{1}H-NMR spectrum of GA-yne-amide

^{1}H-NMR (400Hz, $CDCl_3$, δ, ppm): 12.84 (s, 1H), 7.57 (d, 1H), 6.89 (t, 1H), 6.68 (m, 1H), 5.47 (m, 1H), 5.39 (m,2H) 5.04 (m, 2H), 4.06 (m, 1H), 3.98 (m, 1H), 3.48 (t, 1H), 3.28 (m, 1H), 3.16 (m, 1H), 2.71 (m, 1H), 2.56 (d, 1H), 2.41 (m, 1H), 2.34 (m, 1H), 2.18 (m, 1H), 2.05 (m, 2H) 1.81 (s, 3H), 1.73 (s, 3H), 1.71 (s, 3H), 1.65 (s, 3H), 1.44 (s, 3H), 1.41 (s, 3H), 1.36 (s, 3H), 1.30 (s, 3H), 1.23 (s, 3H)

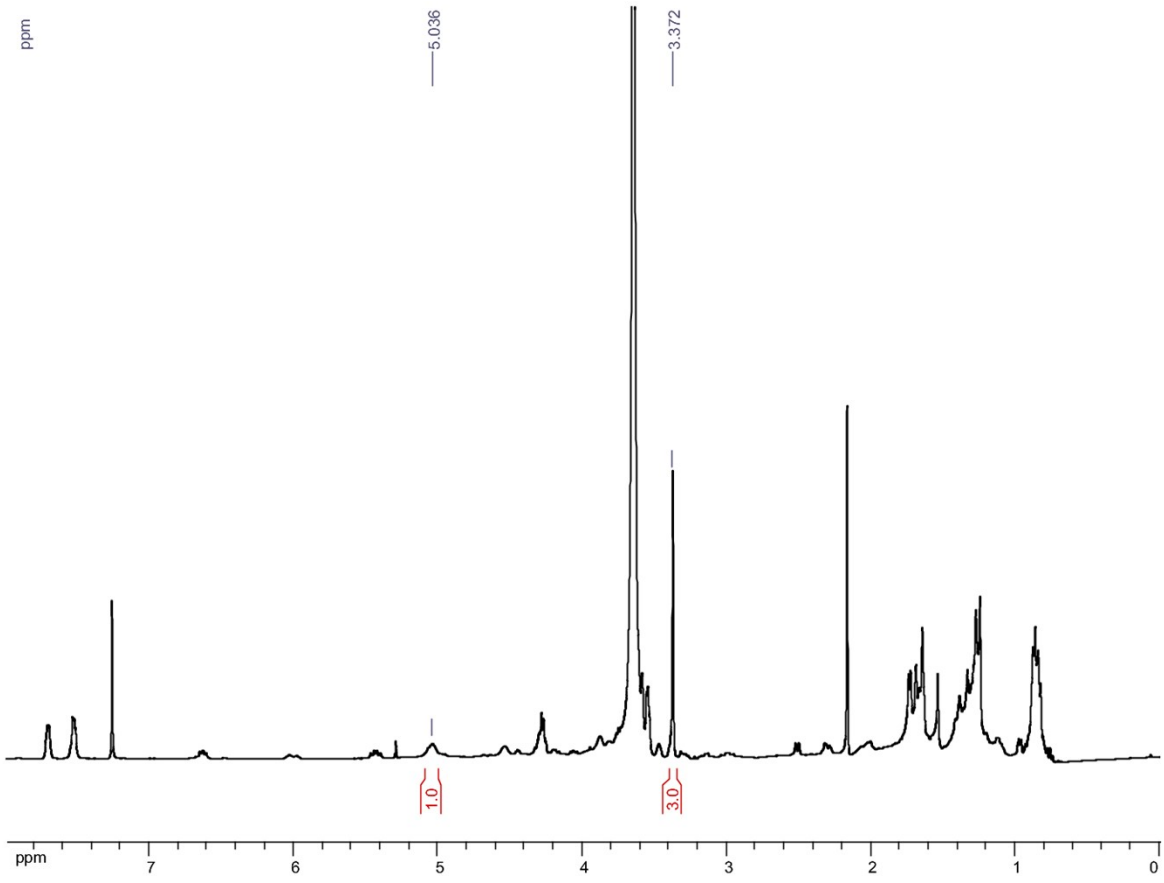

Figure S4. ^{1}H-NMR mPEG$_{550}$-ester-GA

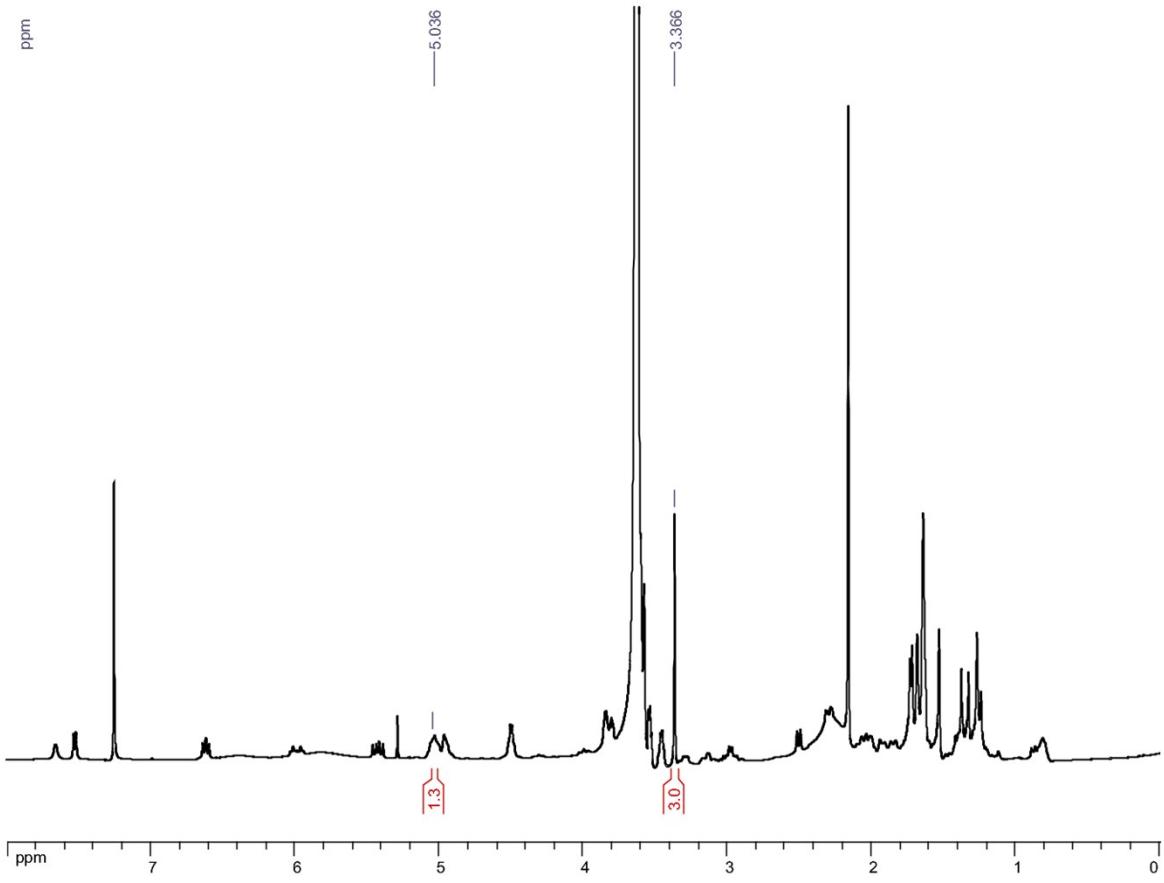

Figure S5. ^{1}H-NMR mPEG$_{2000}$-ester-GA

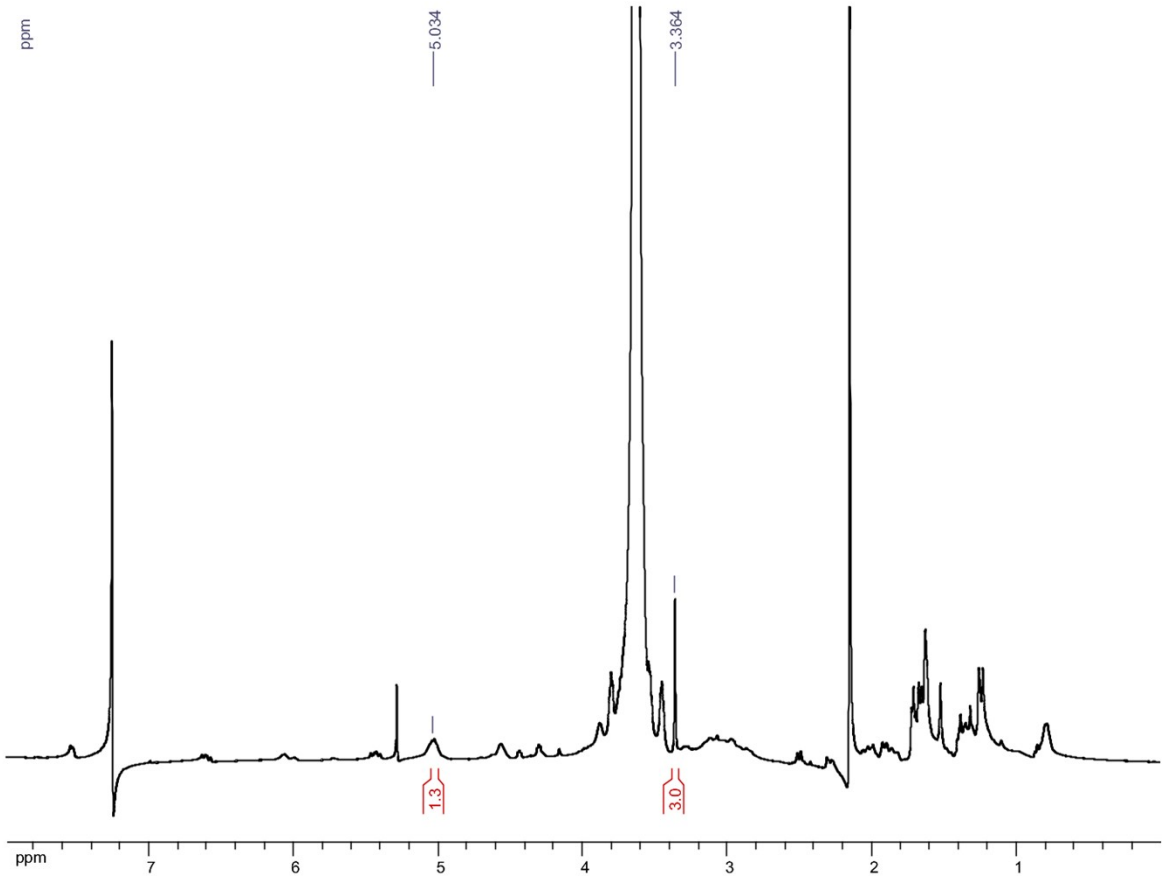

Figure S6. ^{1}H-NMR mPEG$_{5000}$-ester-GA

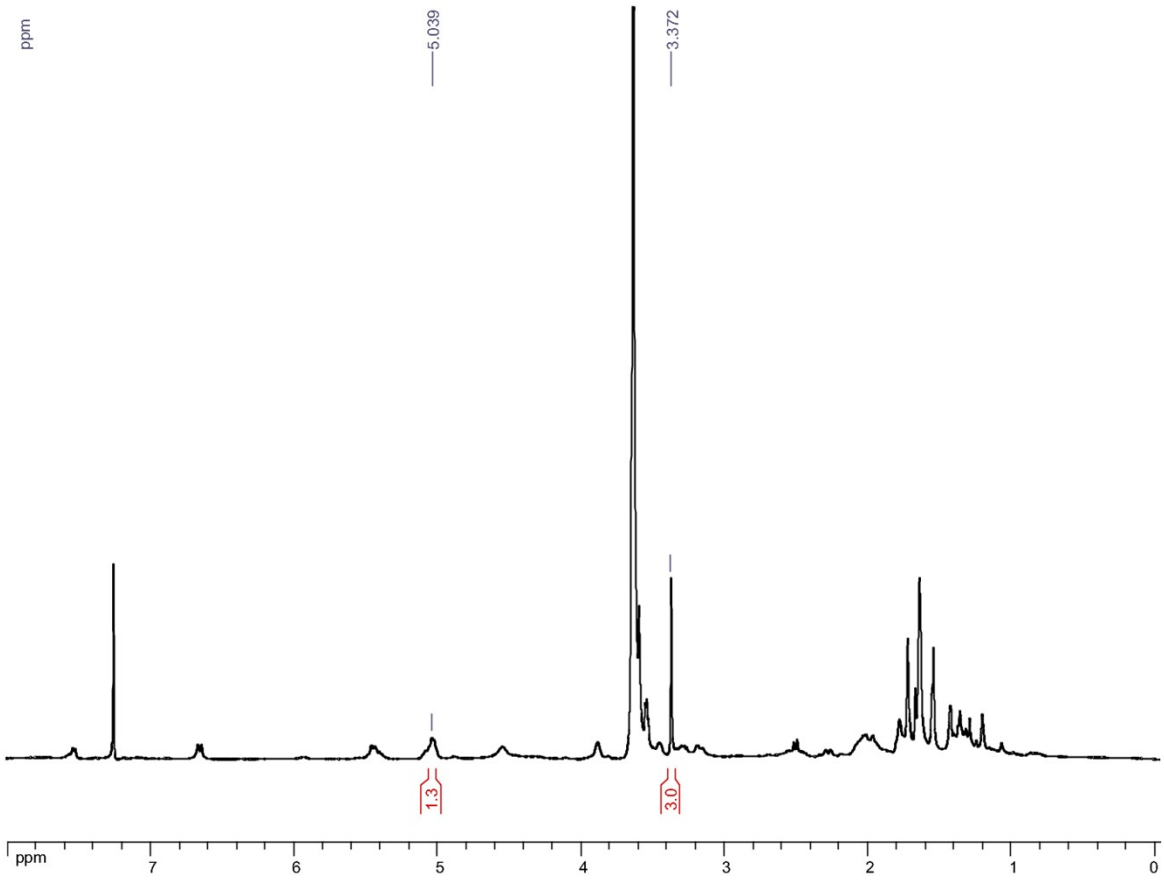

Figure S7. ^{1}H-NMR mPEG$_{550}$-amide-GA

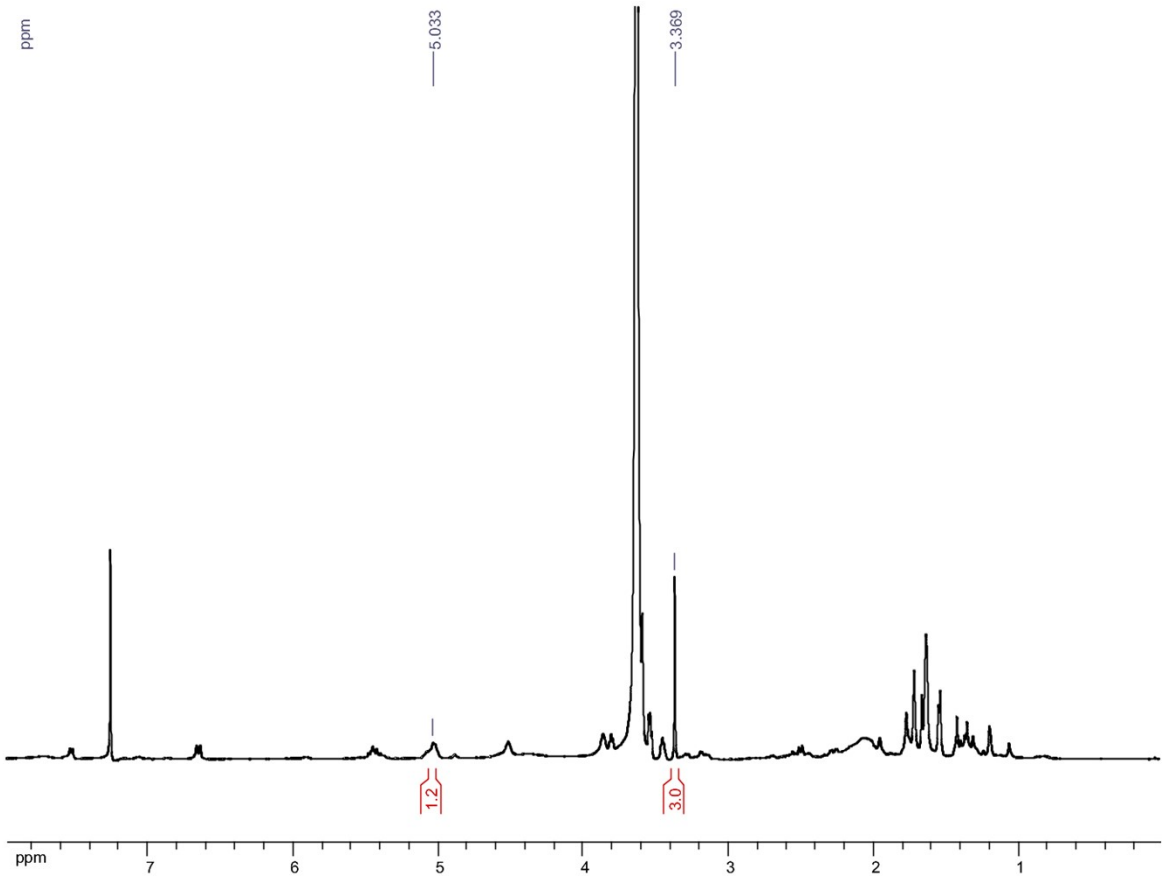

Figure S8. ^{1}H-NMR mPEG$_{2000}$-amide-GA

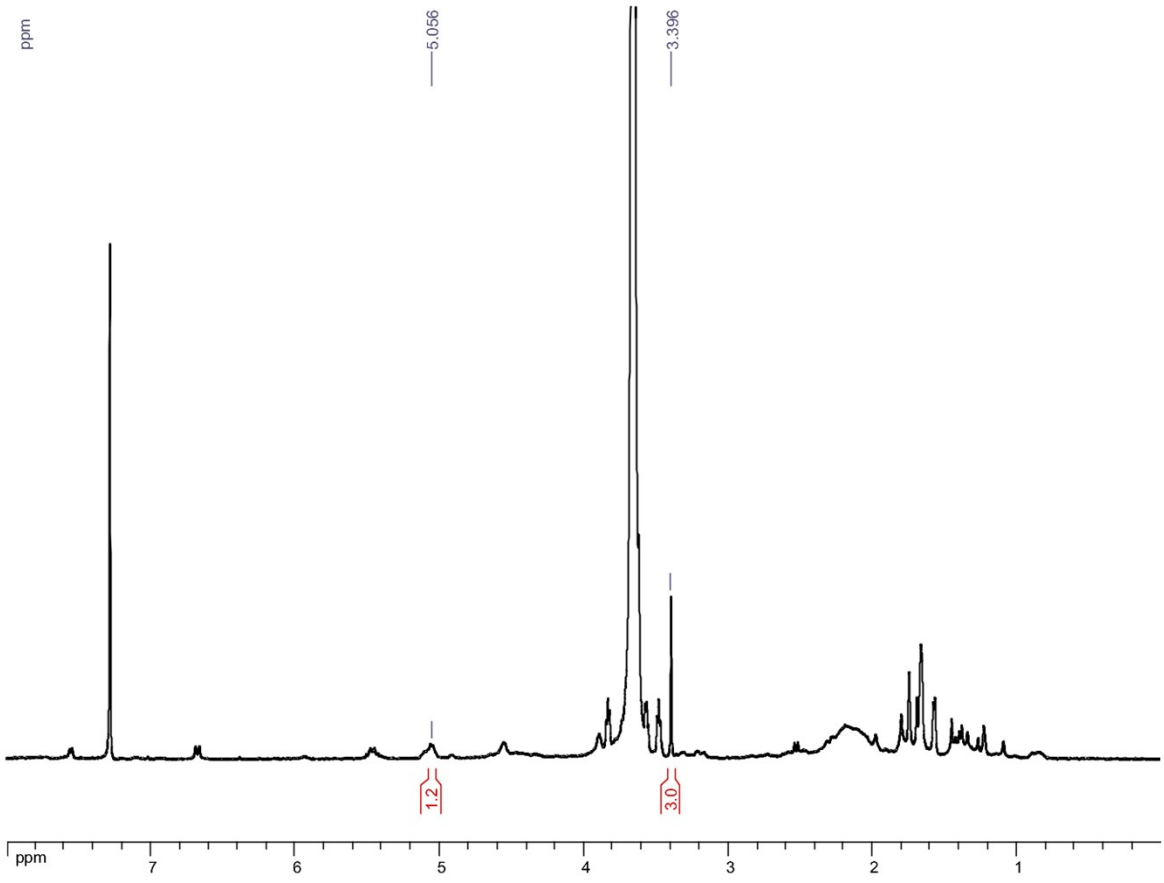

Figure S9. ^{1}H-NMR mPEG$_{5000}$-amide-GA

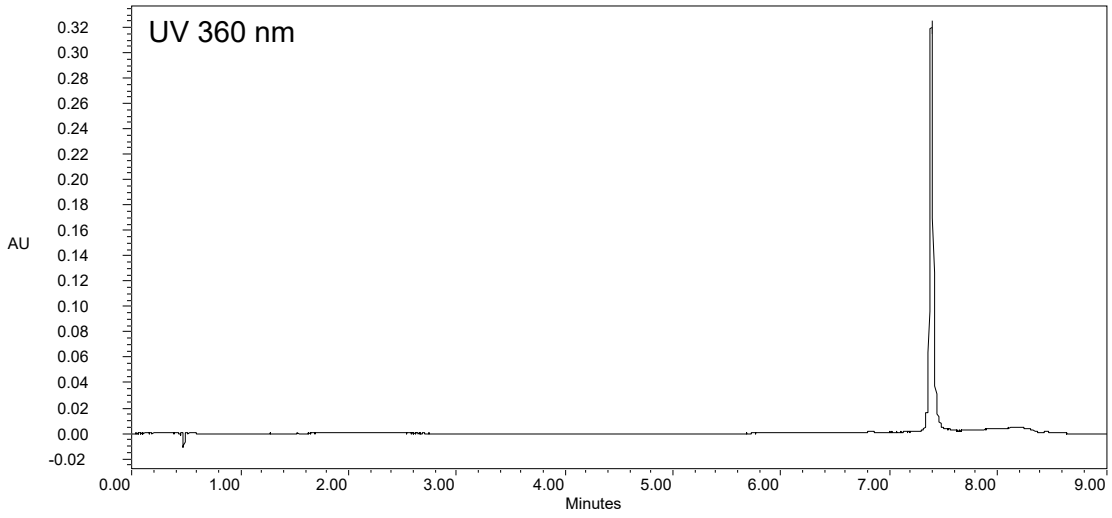

Figure S10. Chromatogram of GAyne-ester, 7.387 minutes

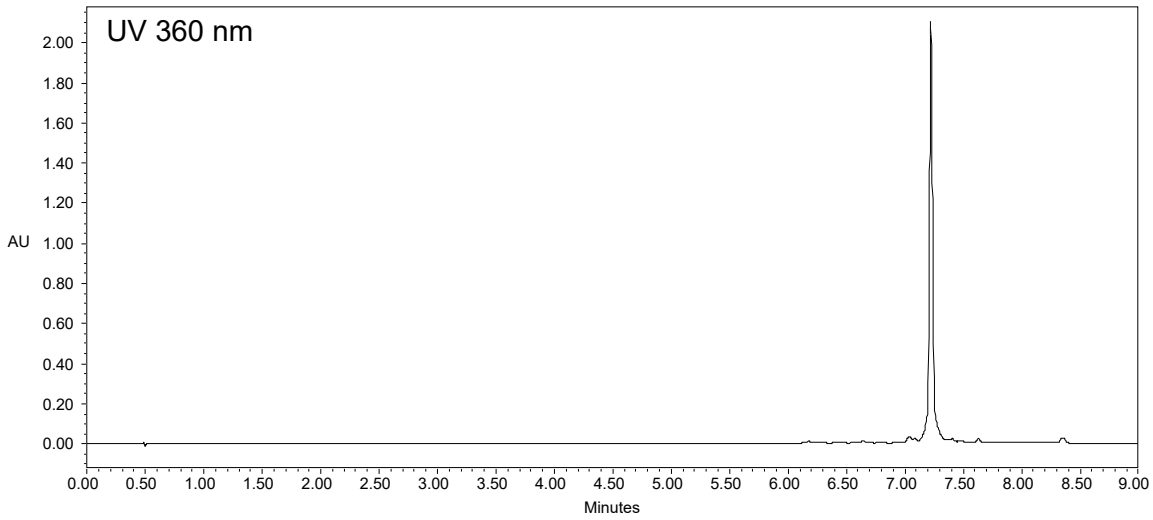

Figure S11. Chromatogram of GAyne-amide, 7.225 minutes

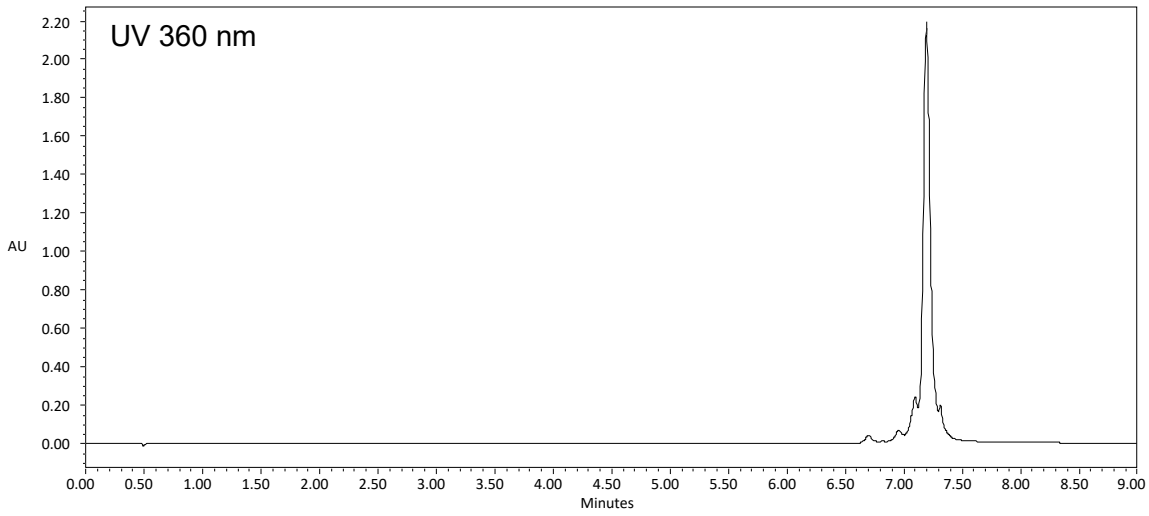

Figure S12. Chromatogram of mPEG550-ester-GA, 7.195 minutes

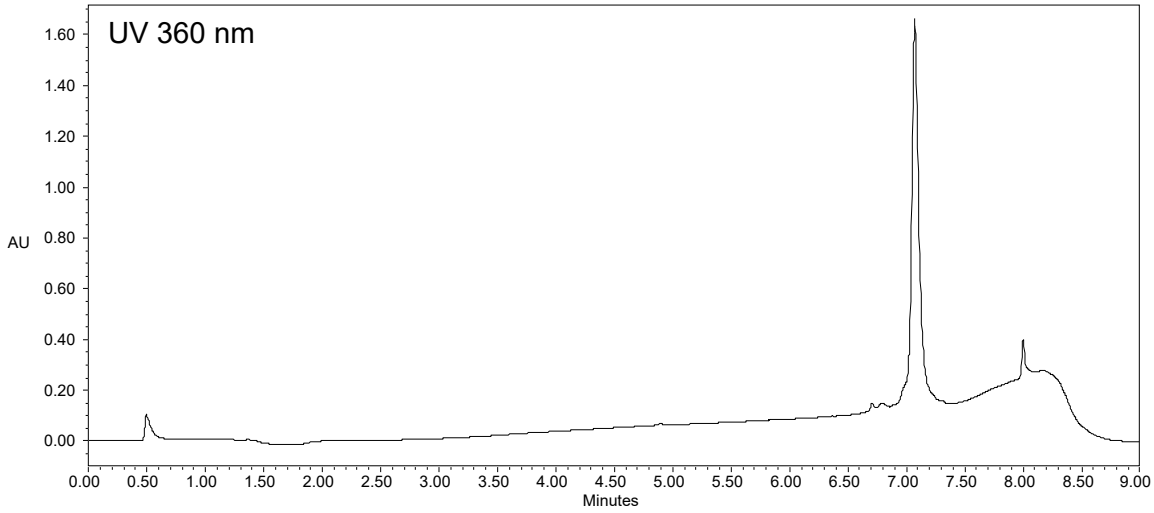

Figure S13. Chromatogram of mPEG2000-ester-GA, 7.073 minutes

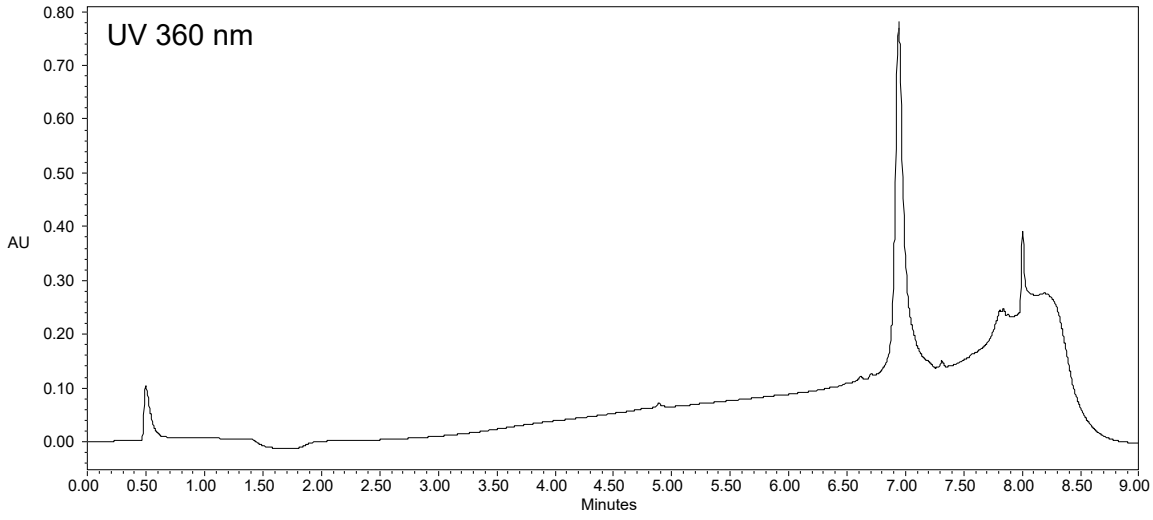

Figure S14. Chromatogram of mPEG2000-ester-GA, 7.073 minutes

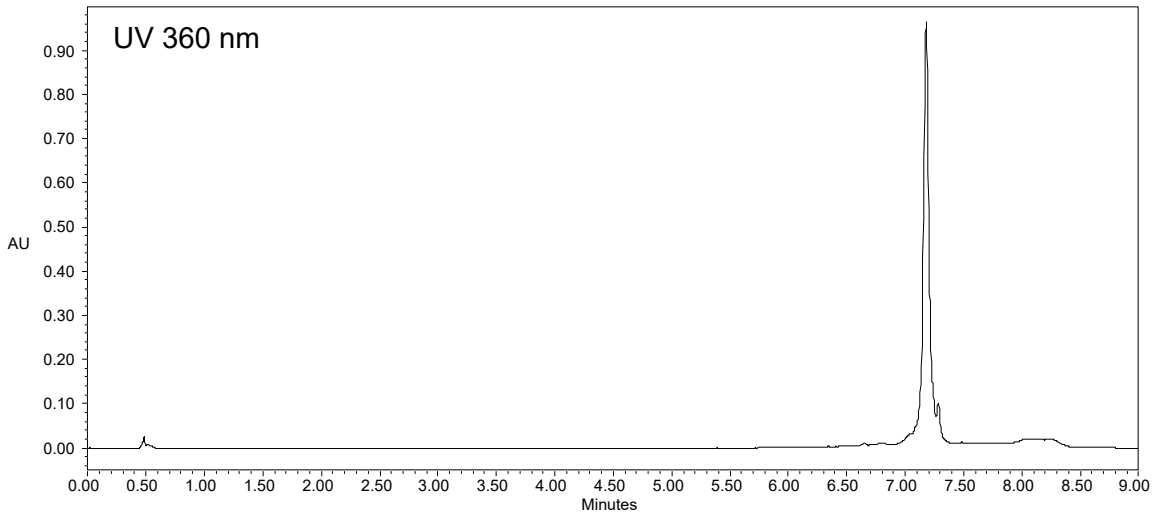

Figure S15. Chromatogram of mPEG550-amide-GA, 7.178 minutes

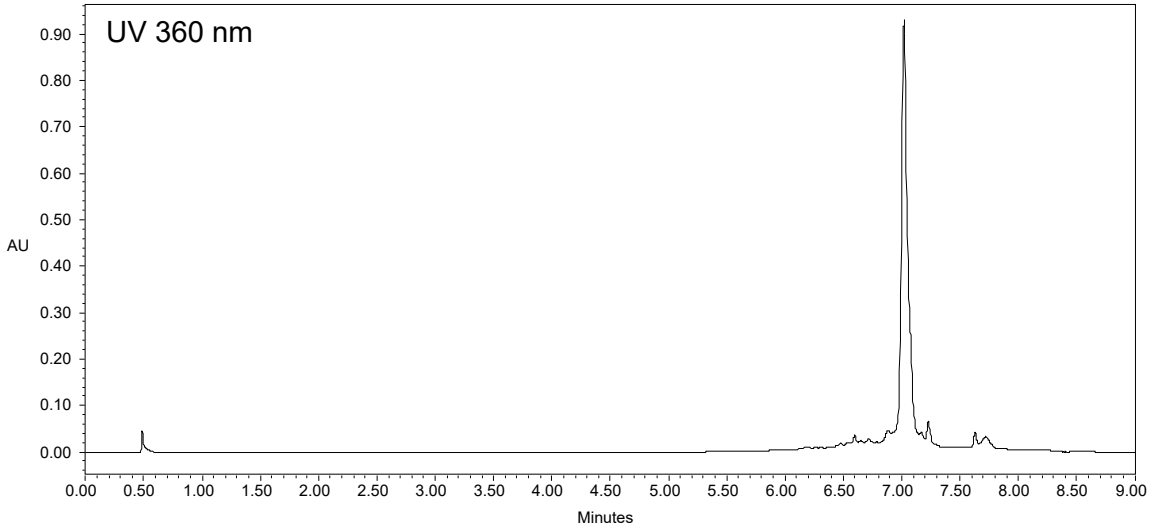

Figure S16. Chromatogram of mPEG2000-amide-GA, 7.018 minutes

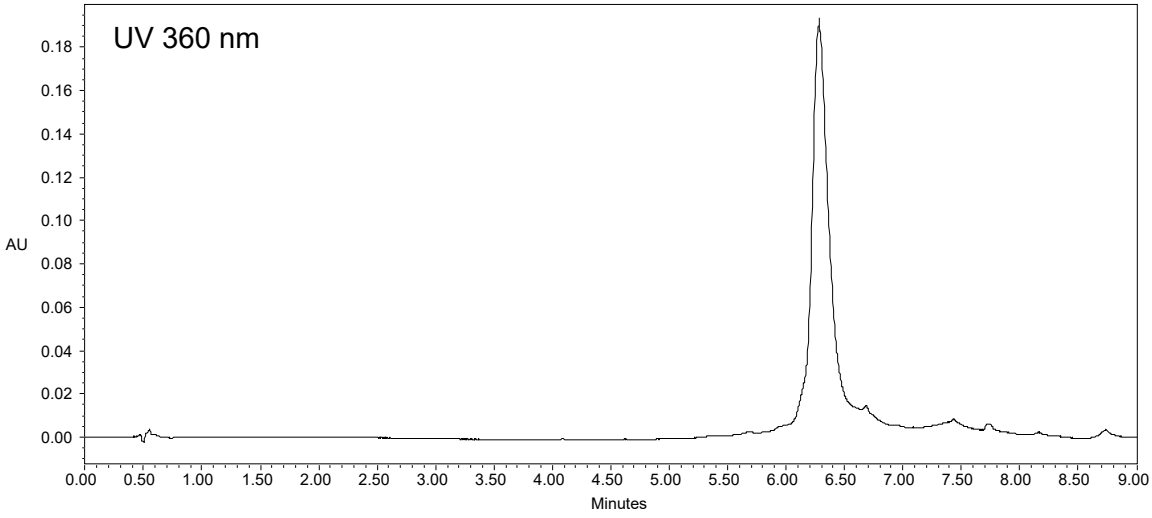

Figure S17. Chromatogram of mPEG5000-amide-GA, 6.280 minutes

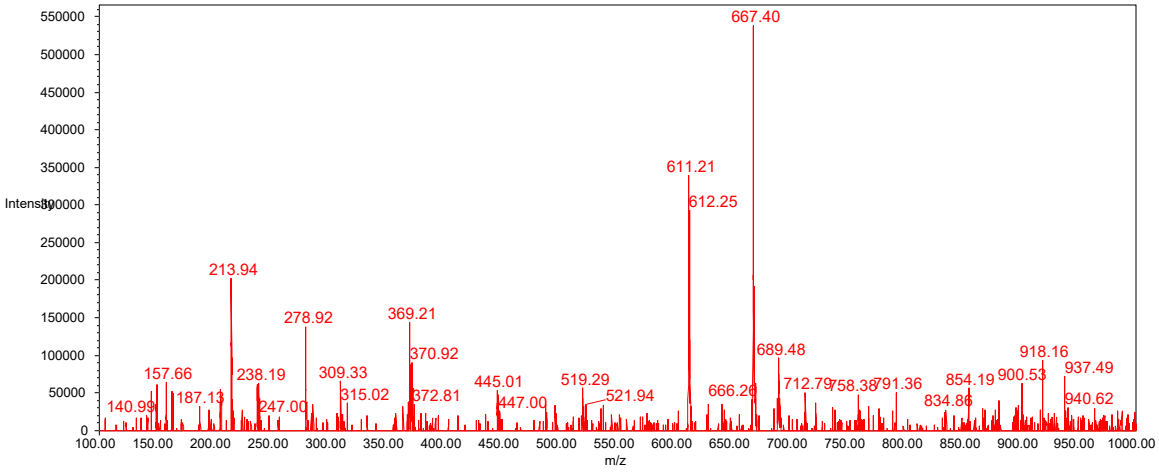

Figure S18. Mass spectrum of GAyne-ester

Calculated $[M+H]^+$ $C_{41}H_{47}O_8$: 667.32

Measured $[M+H]^+$ = 667.40

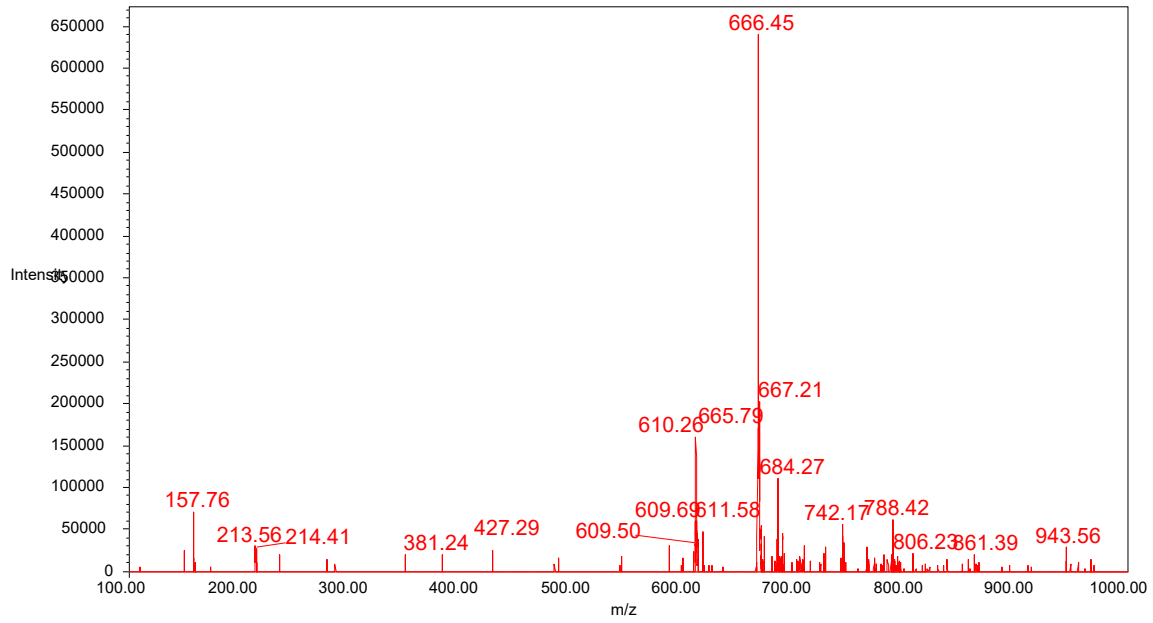

Figure S19. Mass spectrum of GAyne-amide

Calculated $[M+H]^+$ $C_{41}H_{47}NO_7$: 665.34

Measured $[M+H]^+$ = 666.45

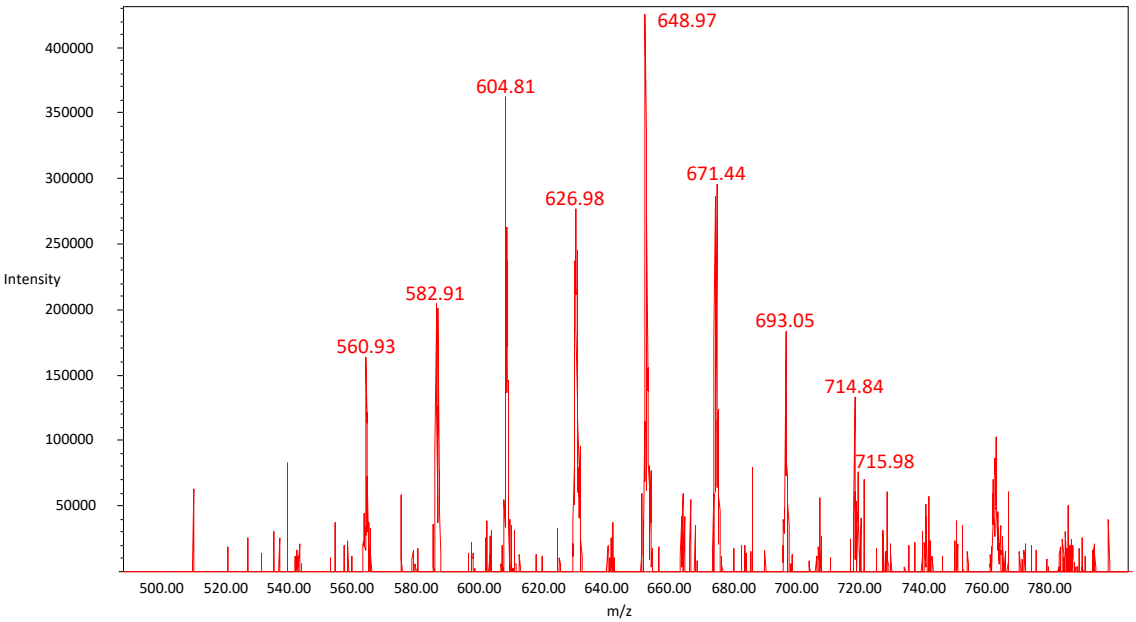

Figure S20. Mass spectrum of mPEG550-ester-GA

Calculated $[M+H]^+$ $(C_{42}H_{49}N_3O_8)$-$(C_2H_4O)_{n=9\text{-}16}$: 560.80, 582.81, 604.83, 626.84, 648.85, 670.87, 692.88, 714.89; Measured [M+H]+ = 560.93, 582.91, 604.81, 626.98, 648.97, 671.44, 693.05, 714.84

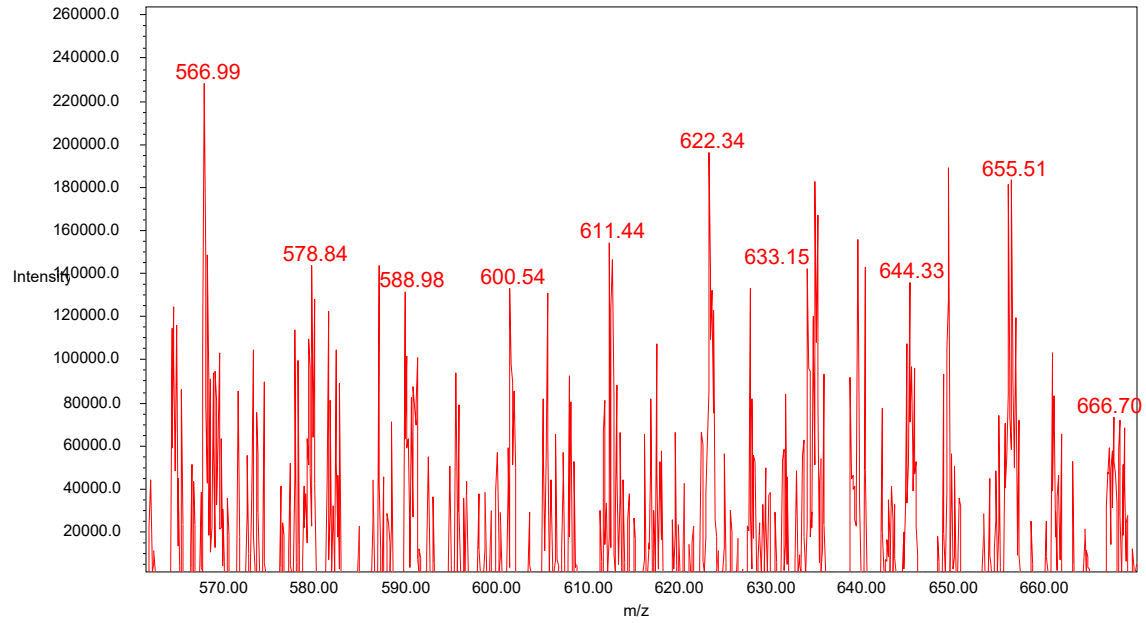

Figure S21. Mass spectrum of mPEG2000-ester-GA

Calculated $[M+4H]^{4+}$ $(C_{42}H_{49}N_3O_8)$-$(C_2H_4O)_{n=35\text{-}44}$: 567.07, 578.08, 589.09, 600.09, 611.10, 622.11, 633.11, 644.12, 655.13, 666.13; Measured $[M+4H]^{4+}$ = 566.99, 578.84, 588.98, 600.54, 611.44, 622.34, 633.11, 644.33, 655.51, 666.70

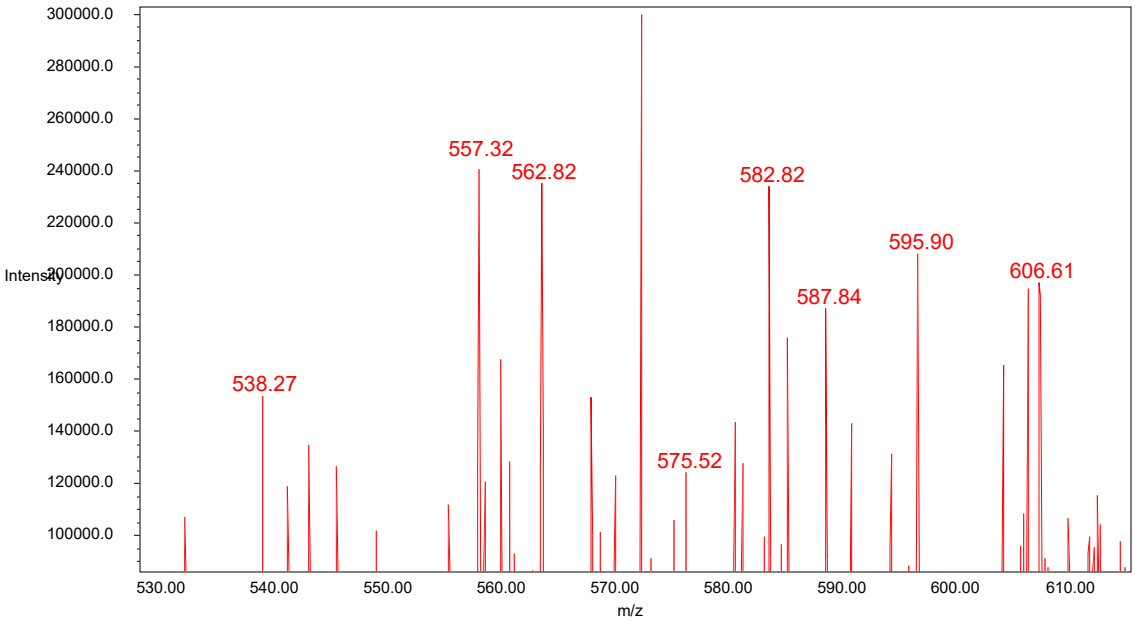

Figure S22. Mass spectrum of mPEG5000-ester-GA

Calculated $[M+8H]^{8+}$ $(C_{42}H_{49}N_3O_8)$-$(C_2H_4O)_{n=69-80}$: 538.32, 557.18, 563.47, 576.06, 582.34, 588.63, 594.92, 607.50; Measured $[M+8H]^{8+}$ = 538.27, 557.32, 582.82, 575.52, 582.82, 587.84, 595.90, 606.61

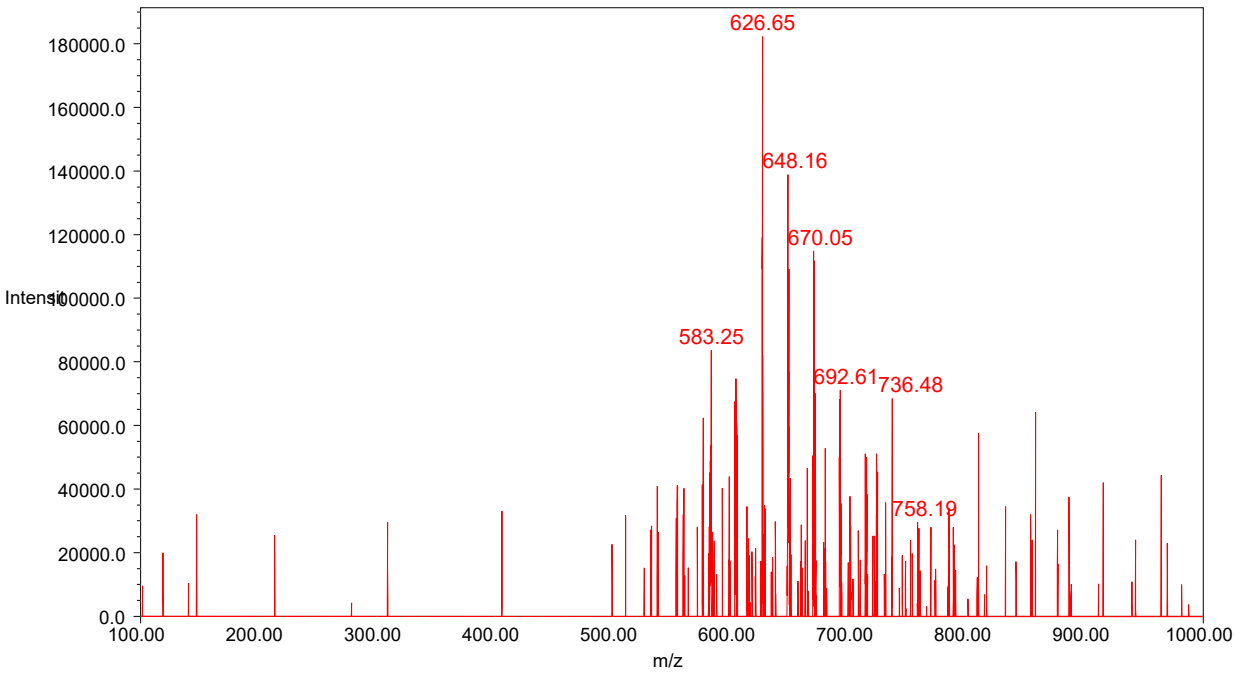

Figure S23. Mass spectrum of mPEG550-amide-GA

Calculated $[M+H]^+$ $(C_{42}H_{50}N_4O_7)$-$(C_2H_4O)_{n=9\text{-}16}$: 582.32, 626.35, 648.36, 670.37, 692.38, 736.41, 758.42; Measured $[M+H]^+$ = 583.25, 626.65, 648.16, 670.05, 692.61, 736.48, 758.42

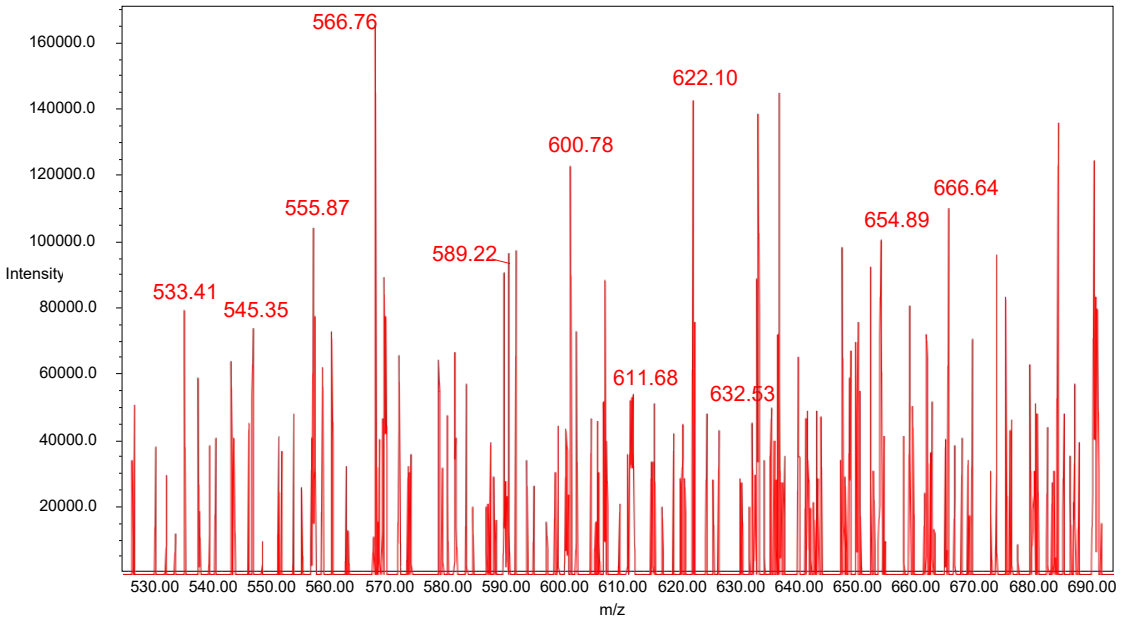

Figure S24. Mass spectrum of mPEG2000-amide-GA

Calculated $[M+4H]^{4+}$ $(C_{42}H_{50}N_4O_7)$-$(C_2H_4O)_{n=32-44}$: 533.8075, 544.81, 555.82, 566.83, 588.84, 599.85, 610.85, 621.86, 632.87, 643.88, 654.88, 665.89; Measured $[M+4H]^{4+}$ = 533.41, 545.35, 555.87, 566.76, 589.22, 600.78, 611.68, 622.10, 632.53, 654.89, 666.64

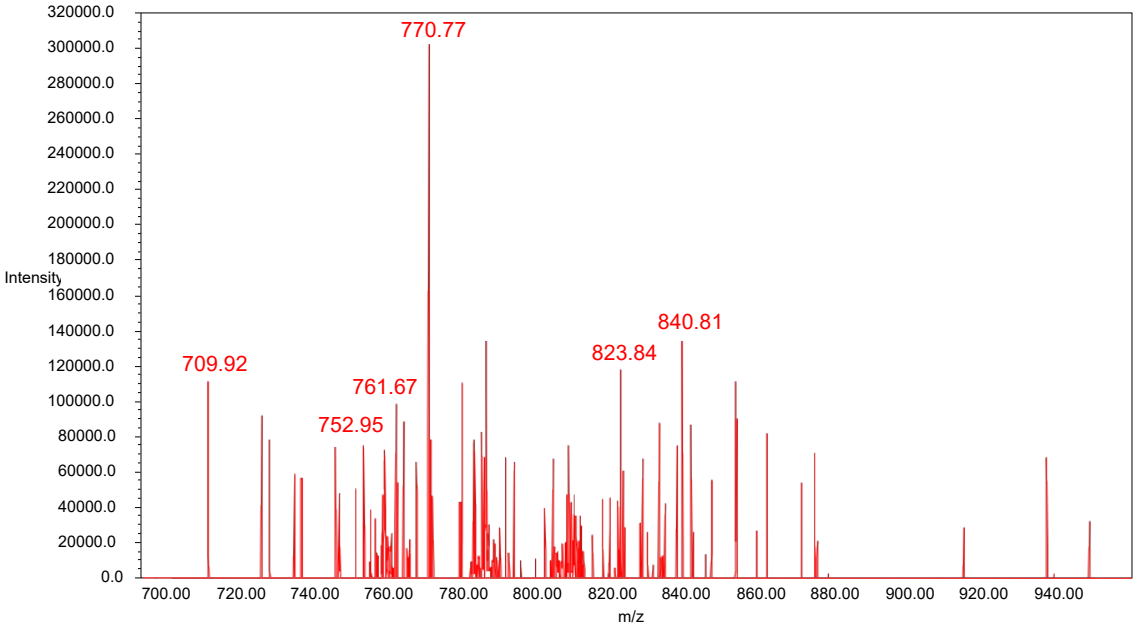

Figure S25. Mass spectrum of mPEG5000-amide-GA
Calculated $[M+4H]^{4+}$ $(C_{42}H_{50}N_4O_7)$-$(C_2H_4O)_{n=64\text{-}79}$: 709.02, 753.04, 761.85, 770.65, 823.48, 841.09; Measured $[M+4H]^{4+}$ = 709.92, 752.95, 761.67, 770.77, 823.84, 840.81

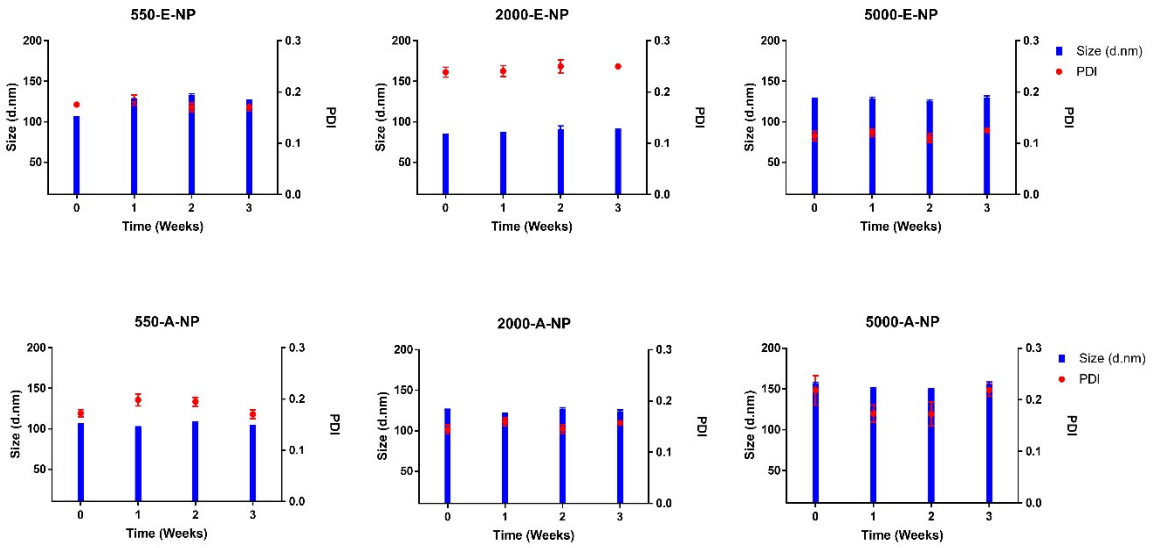

Figure S26. Stability of GA-NPs over three weeks. Data = mean ± SD (n = 3).