Supporting Information

Design and Synthesis of a Fluorescent Amino Poly (glycidyl methacrylate) for Efficient Gene Delivery

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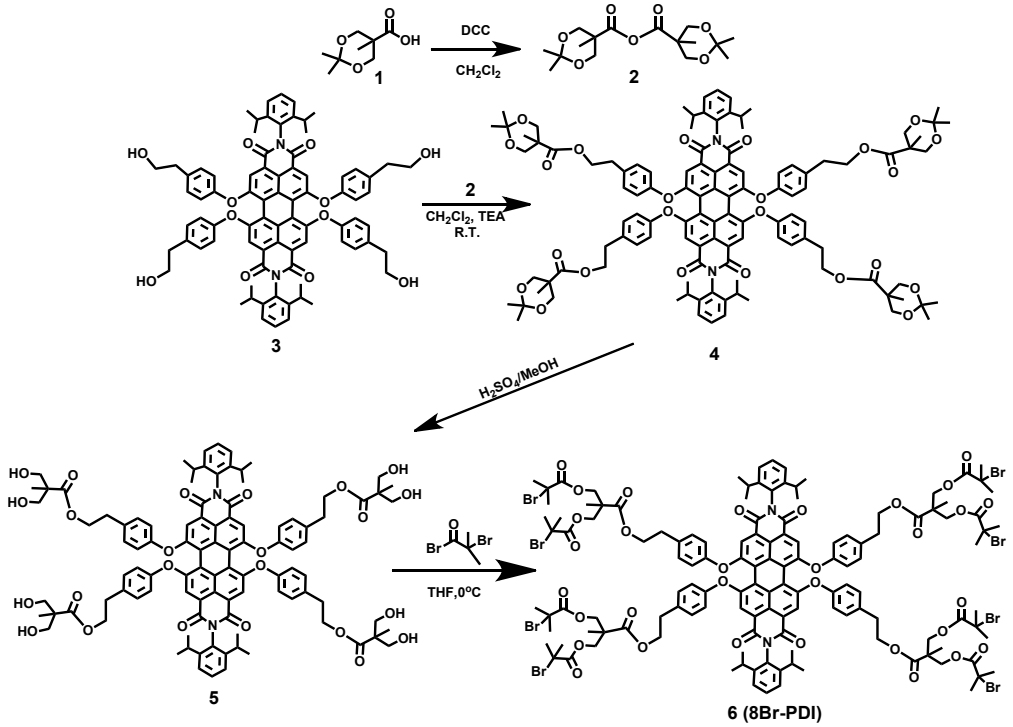

Scheme S1 Synthesis route of the initiator 8Br-PDI. Before polymer synthesis, we synthesized the ATRP initiator (8Br-PDI) first. The intermediate products were well characterized by NMR and mass spectra.

Experiments

Materials and instruments

Dichloromethane and triethylamine (TEA) were distilled from CaH_2 under a nitrogen atmosphere immediately prior to use. Isopropylidene-2,2-bis(oxymethyl) propionic acid (compound **1**, 99%) was purchased from Nanjing Chemlin Chemical Industry Co.,Ltd. 2-Bromoisobutyryl bromide (Alfa Aesar, 98%) and copper(I) bromide (CuBr, 99.999%) were used without further purification. Compound **2**[1, 2] and **3** were synthesized as previous reports.[3]

Matrix-assisted laser-desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) were determined on Bruker Daltonics Inc. BIFLEX III MALDI-TOF mass spectrometer.

Synthesis of compound 4

Compound **4** was obtained by esterification of **2** and **3**. Normally, **3** (100 mg, 0.08 mmol) and TEA (0.23 mL, 1.6 mmol) were dissolved in dry CH_2Cl_2 and cooled to 0°C. The solution of **2** (1.06 g, 3.2 mmol) in dry CH_2Cl_2 was added dropwise under vigorous stirring. The mixture was stirred under a nitrogen atmosphere and monitored by TLC. After 24 h, the mixture was diluted by excess CH_2Cl_2 and washed with $NaHSO_4$ (3×30 ml, 1 M) and sat. aq. NaCl (2 ×30 ml). The organic phase was dried with $MgSO_4$, filtered and the filtrate evaporated under vacuum. The crude product was purified by silica column chromatography using CH_2Cl_2/EtOAc (3:1) as the eluent. Compound **4** was obtained as a red powder (135 mg, 90%). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.19 (s, 4H, perylene), 7.41 (t, 2H, Ph-*H*), 7.26 (d, 4H, Ph-*H*), 7.13 (d, 8H, Ph-*H*), 6.89 (d, 8H, Ph-*H*), 4.30 (t, 8H, -*CH*$_2$COO), 4.14 (d, 4H, -*CH*$_2$-O), 3.77 (d, 4H, -*CH*$_2$-O), 3.61 (t, 8H, Ph-*CH*$_2$-), 2.95 (t, 8H, -*CH*$_2$-O), 2.67 (t, 8H, -*CH*$_2$-O), 2.17 (s, 12H, acetonide-*CH*$_3$), 1.41 (d, 6H, -*CH*$_3$), 1.37 (d, 6H, -*CH*$_3$), 1.11 (d, 24H, Ph-CH-(*CH*$_3$)$_2$), 1.15 (d, 6H, acetonide- *CH*$_3$), 1.02 (d, 6H, acetonide- *CH*$_3$). MS (MALDI-TOF) m/z Calculated for $[M+H]^+$=1880.8497, $[M+Na]^+$=1902.8317, $[M+K]^+$=1918.8056; Found: 1880.2, 1902.3, 1918.2.

Synthesis of compound 5

Compound **4** (100 mg, 0.053 mmol) was dissolved in MeOH (5 ml) and H_2SO_4 (0.4 ml, conc. = 2% v/v) was added at room temperature. The reaction was stirred followed by TLC until completion (~4 h) then neutralised using NH_4OH in MeOH (10 ml, 50:50 v/v) resulting in ammonium sulfate being produced as a white precipitate. This was left stirring for 30 min. The salt was removed by filtration. The filtrate was evaporated to provide compound 5 as a red solid (87 mg, 95%). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.22 (s, 4H, perylene), 7.46 (t, 2H, Ph-*H*), 7.30 (d, 4H, Ph-*H*), 7.16 (d, 8H, Ph-*H*), 6.97 (d, 8H, Ph-*H*), 4.37 (t, 8H, -*CH*$_2$COO), 3.80 (d, 4H, -*CH*$_2$-OH), 3.67 (t, 8H, Ph-*CH*$_2$-), 2.97 (t, 8H, -*CH*$_2$-OH), 2.68 (t, 4H, Ph-*CH*-(CH_3)$_2$), 2.21 (br, 8H, -*OH*), 1.12 (d, 24H, Ph-CH-(*CH*$_3$)$_2$), 1.05 (d, 6H, -*CH*$_3$).

MS (MALDI-TOF) m/z Calculated for $[M+H]^+$=1720.7245, $[M+Na]^+$=1742.7065, $[M+K]^+$=1758.6804; Found: 1720.5623, 1742.5490, 1758.5135.

Synthesis of compound 6

2-Bromoisobutyryl bromide (0.58 mL, 4.64 mmol) was added dropwise into the solution of compound **5** (100 mg, 0.058 mmol) in dry CH_2Cl_2 (20 mL) and triethylamine (0.73 mL) at 0 ^oC. After stirring for 24 hours, the reaction was quenched with methanol in ice bath. After removing the solvent, the crude product was purified by flash chromatography (silica gel, n-hexane/EtOAc (1:1)) to afford desired product compound **6** (150 mg, 88.7%) as a red powder. ^1H NMR (400 MHz, $CDCl_3$, 25 ^oC): δ= 8.24 (s, 4 H, perylene), 7.43 (t, 2 H, Ph-H),7.29 (d, 4 H, Ph-H),7.15 (d, 8 H, Ph-H), 6.95 (d, 8 H, Ph-H), 4.44 (t, 8H, -*CH*$_2$COO), 4.38 (d, 4H, -*CH*$_2$-OOC), 4.36 (d, 4H, -*CH*$_2$-OOC), 4.34 (t, 8H, Ph-*CH*$_2$-), 2.96 (t, 8H, -*CH*$_2$-OOC), 2.69 (t, 4H, Ph-*CH*-$(CH_3)_2$), 1.91 (s, 48H, -*CH*$_3$ isobutyrate), 1.32 (s, 12H, -*CH*$_3$)1.12 (d, 24H, -*CH*$_3$ isopropyl). ^{13}C NMR (600 MHz, $CDCl_3$, 25 ^oC): δ= 172.22, 170.95, 163.11, 155.82, 154.14, 145.59, 133.63, 130.45, 123.89, 122.95, 120.70, 120.06, 66.25, 66.08, 65.71, 55.41, 46.67, 42.11, 34.29, 30.65, 29.08, 26.19, 25.11, 24.03, 18.25, 17.91, 17.74, 17.33.

MS (MALDI-TOF) m/z Calculated for $[M+H]^+$=2907.3385, $[M+Na]^+$=2930.3224, $[M-Br+H]^+$=2827.4236, $[M-Br+Na]^+$=2849.4109; Found: 2907, 2930, 2827, 2849.

Additional Figures

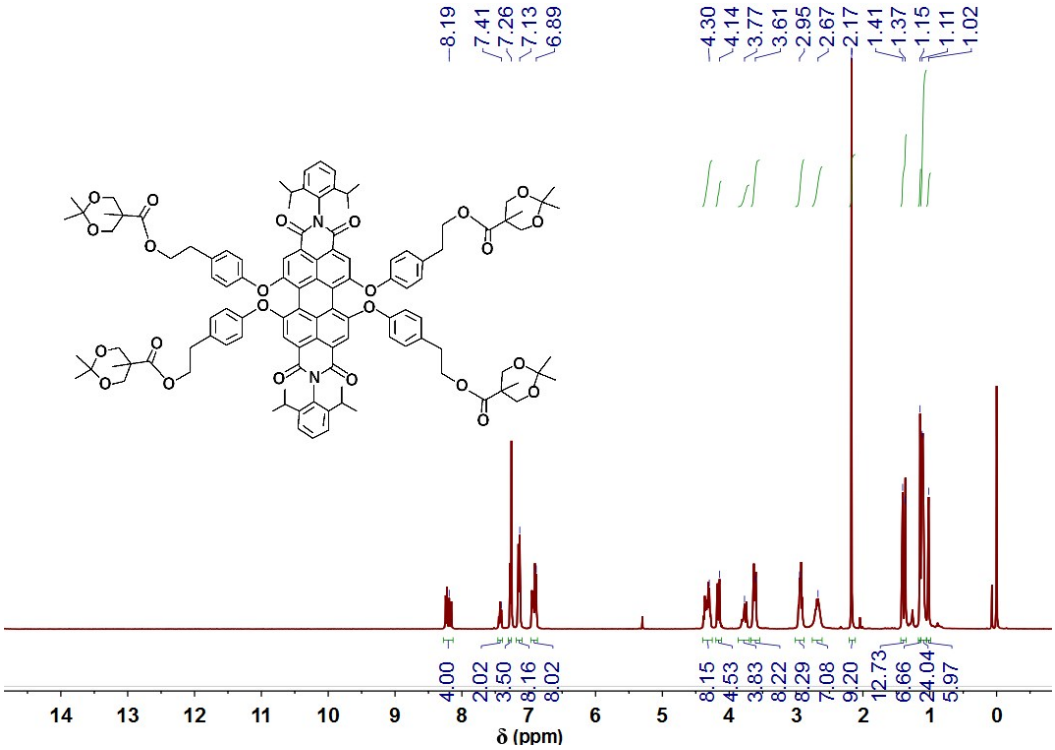

Fig. S1 ^{1}H NMR spectrum of compound 4 in $CDCl_3$.

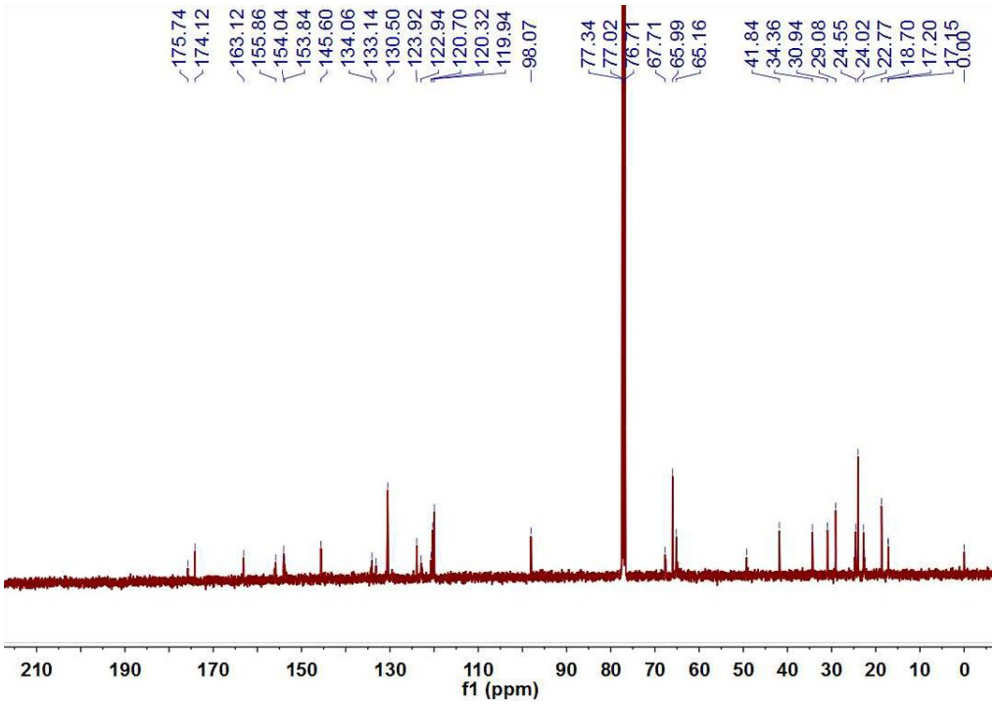

Fig. S2 ^{13}C NMR spectrum of compound 4 in $CDCl_3$.

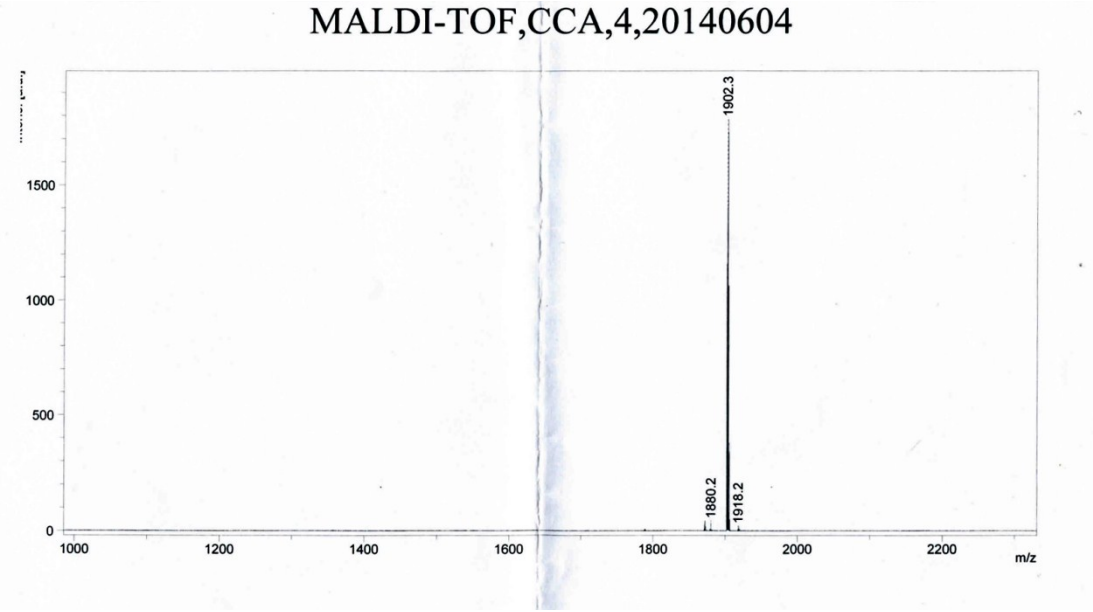

Fig. S3 MALDI-TOF spectrum of compound 4.

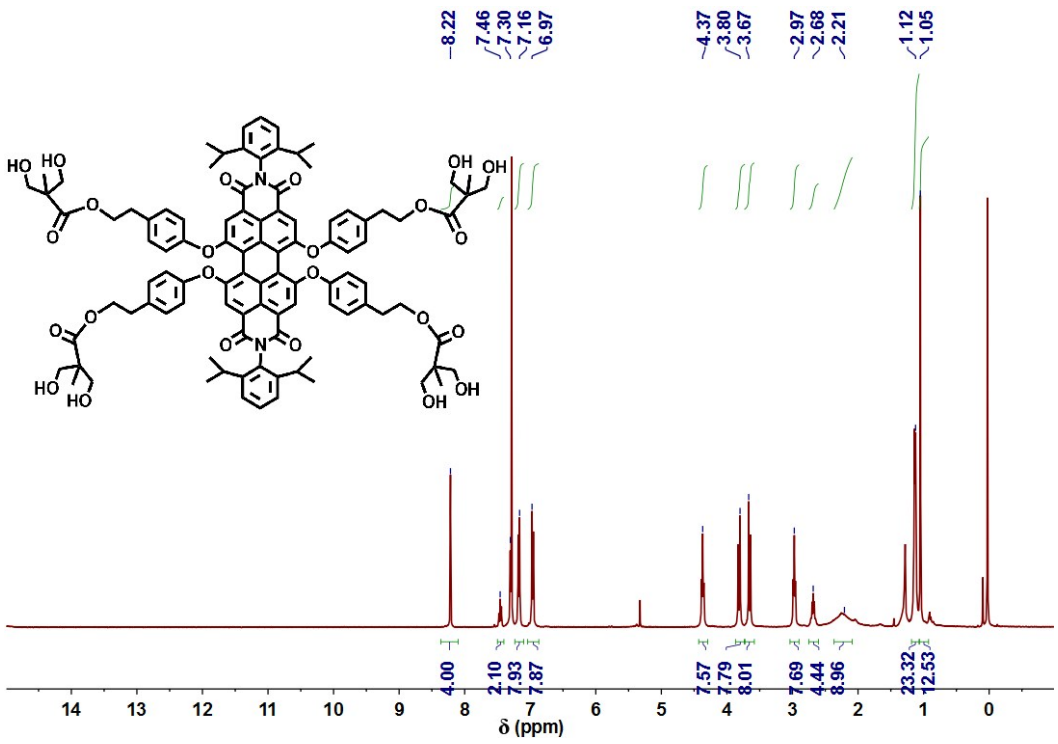

Fig. S4 ^{1}H NMR spectrum of compound 5 in $CDCl_3$.

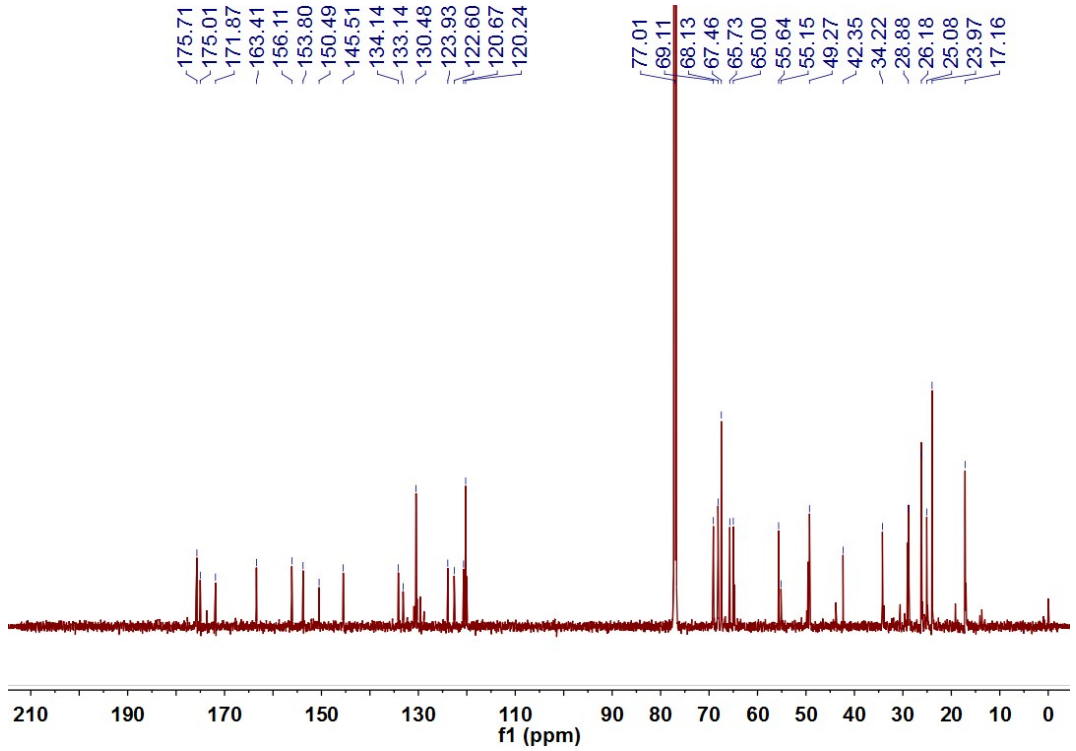

Fig. S5 ^{13}C NMR spectrum of compound 5 in $CDCl_3$.

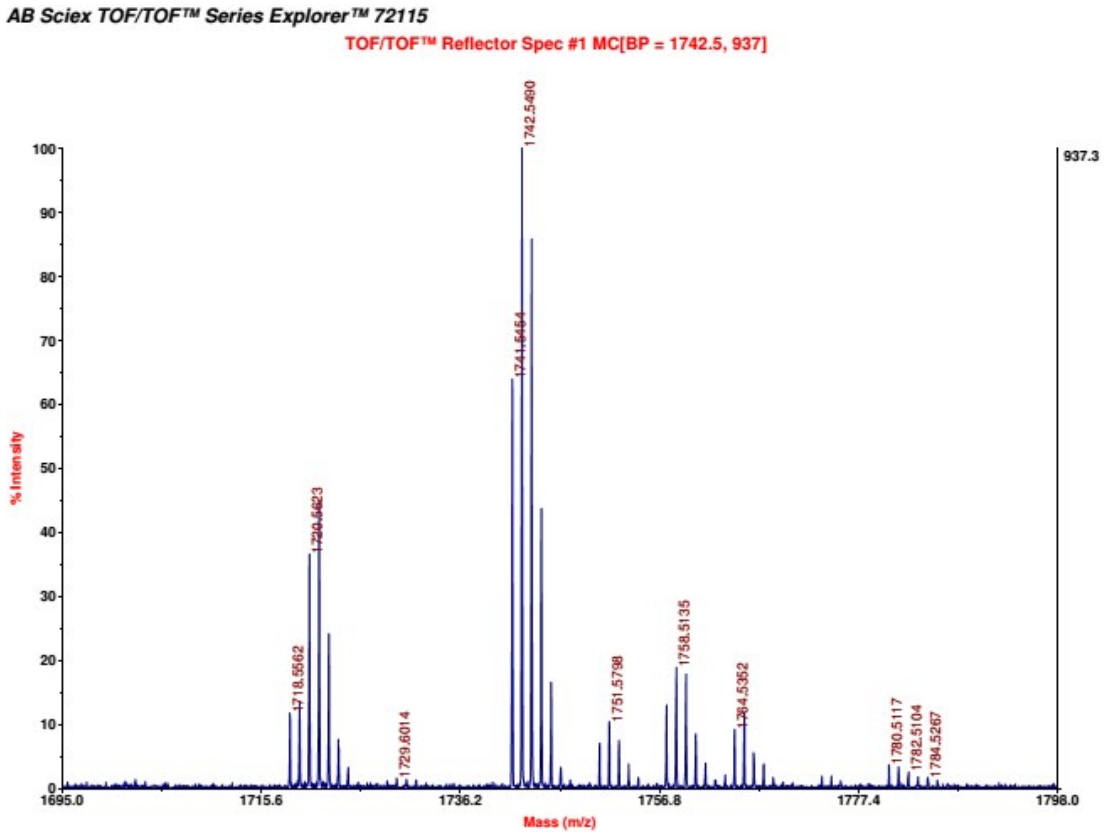

Fig. S6 MALDI-TOF spectrum of compound 5.

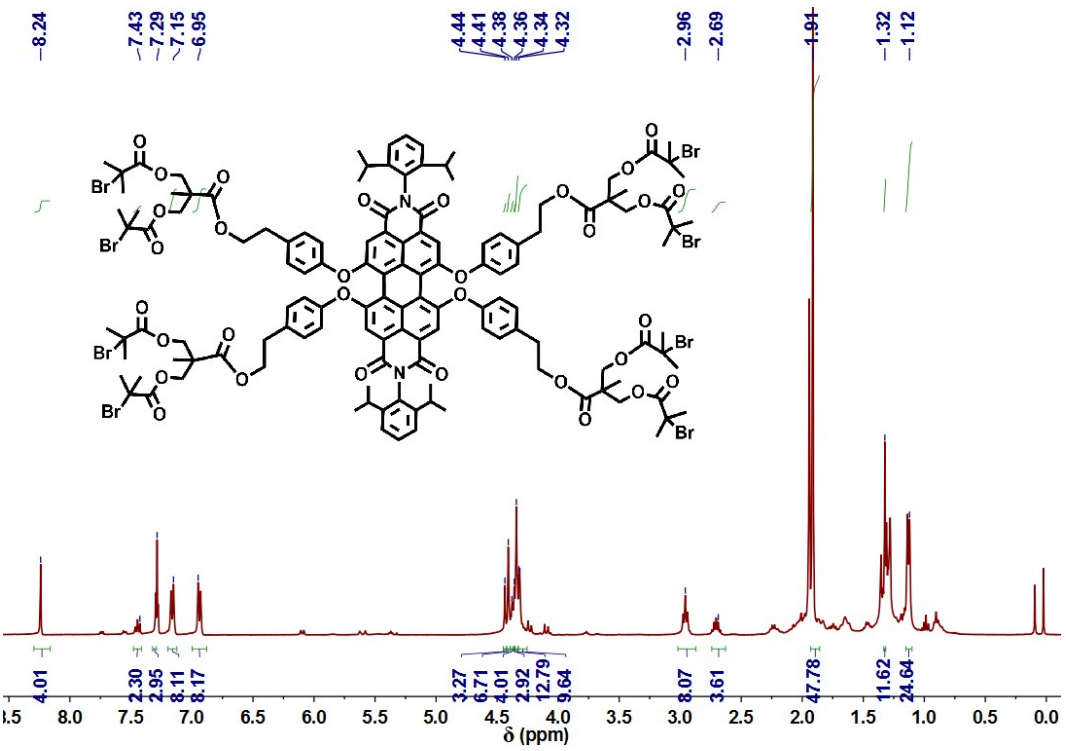

Fig. S7 ^{1}H NMR spectrum of compound 6 (8Br-PDI) in $CDCl_3$.

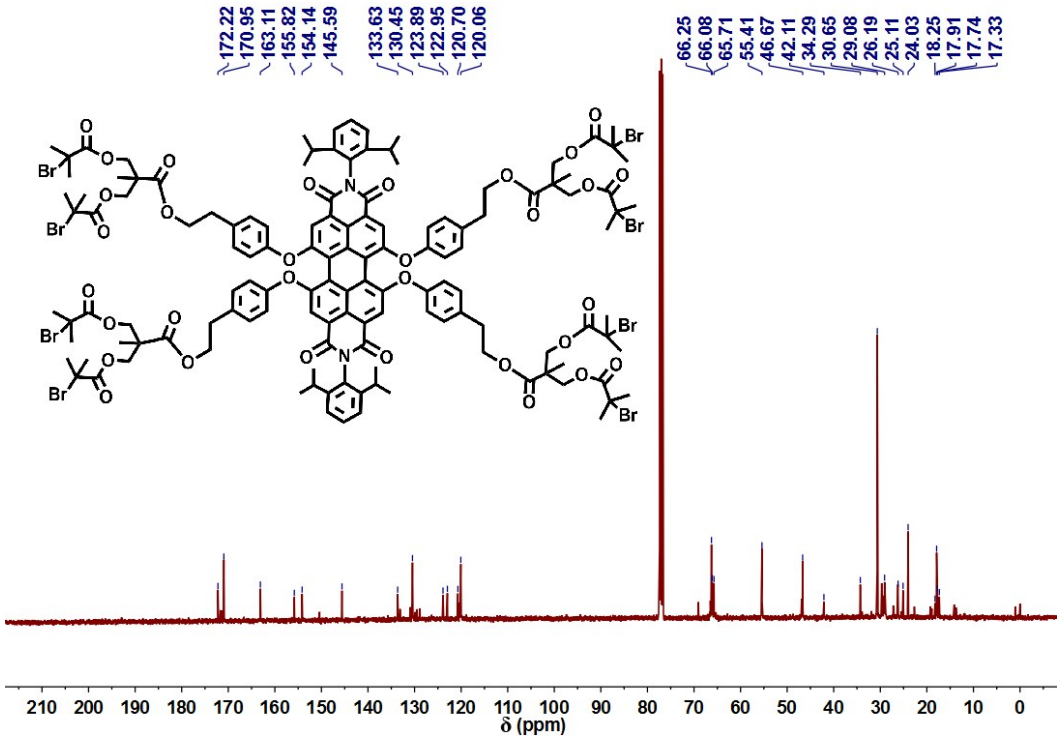

Fig. S8 ^{13}C NMR spectrum of compound 6 (8Br-PDI) in $CDCl_3$.

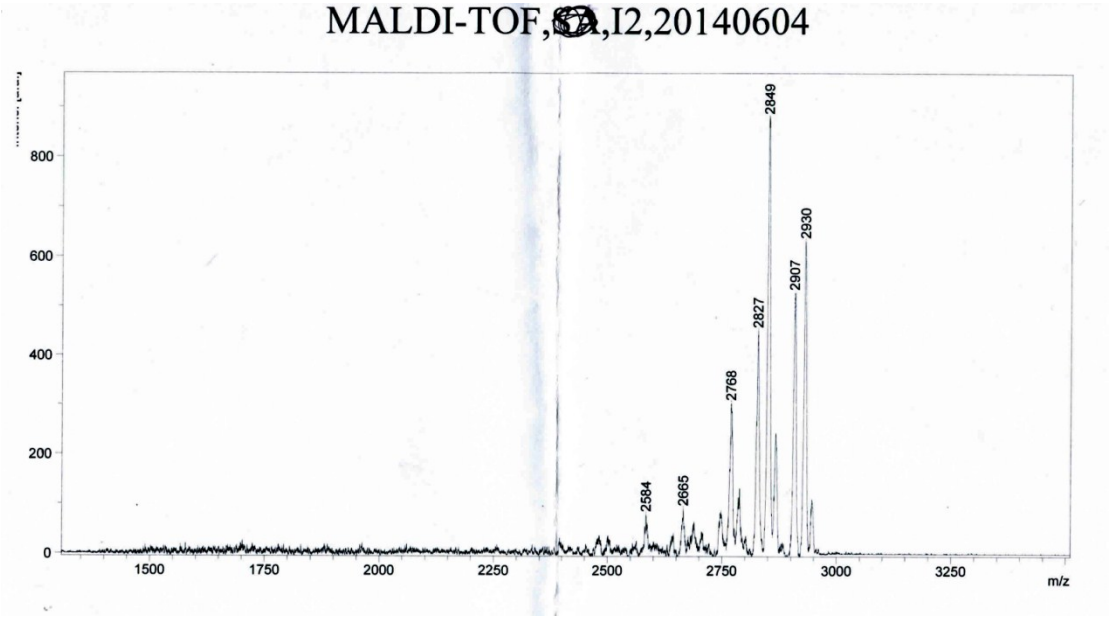

Fig. S9 MALDI-TOF spectrum of compound 6 (8Br-PDI).

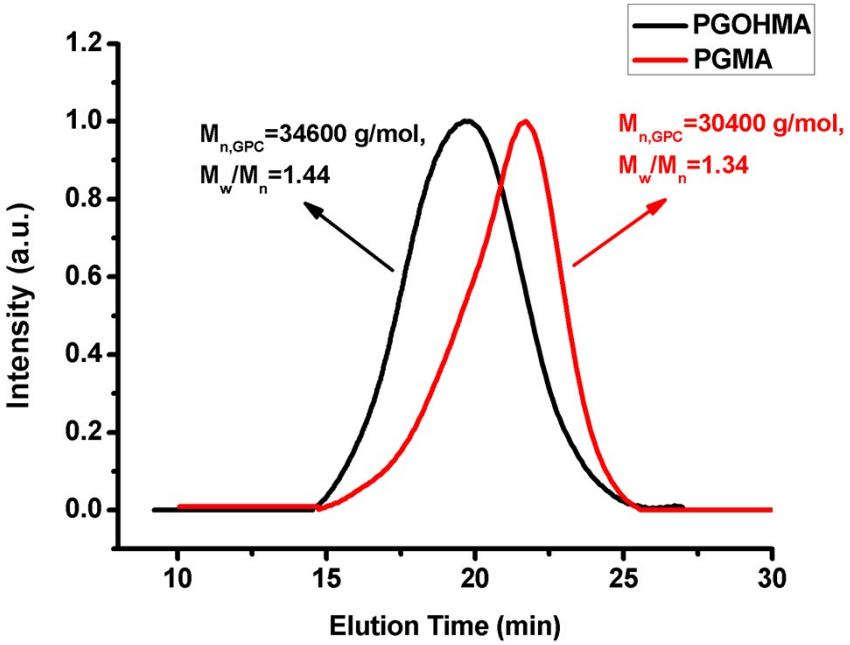

Fig. S10 GPC traces of PGMA and PGOHMA.

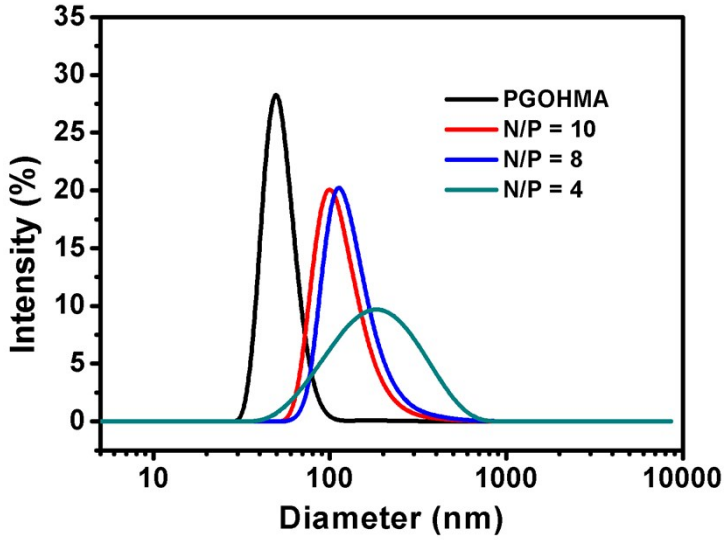

Fig. S11 DLS measurement of PGOHMA/DNA at different N/P ratios.

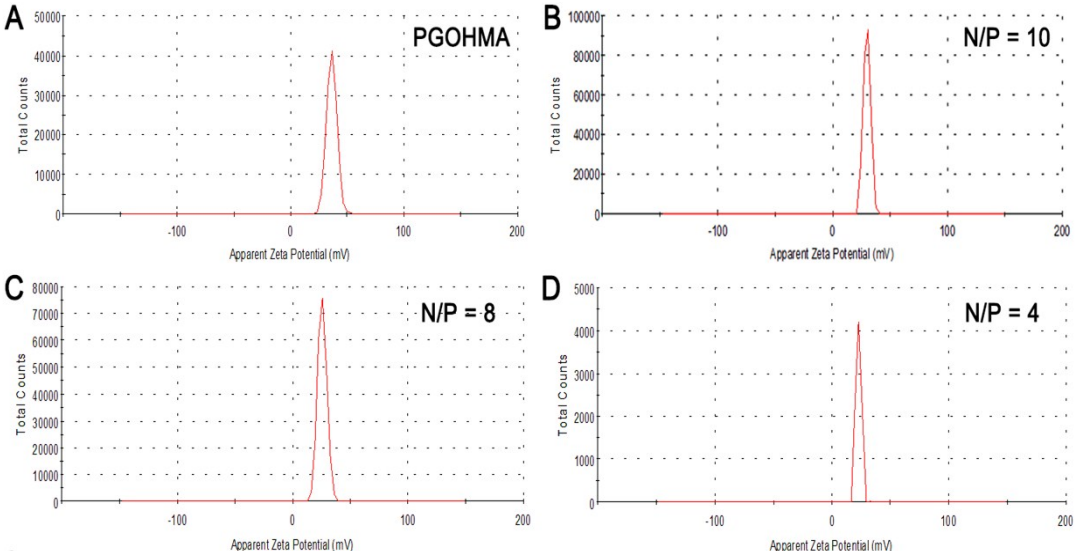

Fig. S12 Zeta potential measurement of PGOHMA/DNA at different N/P ratios.

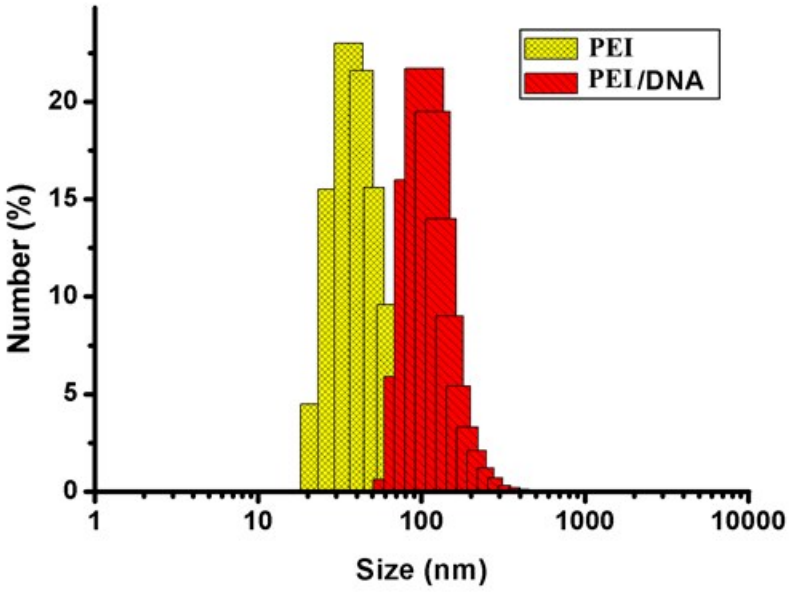

Fig. S13 DLS images of before and after added DNA into PGOHMA (A) and PEI (B).

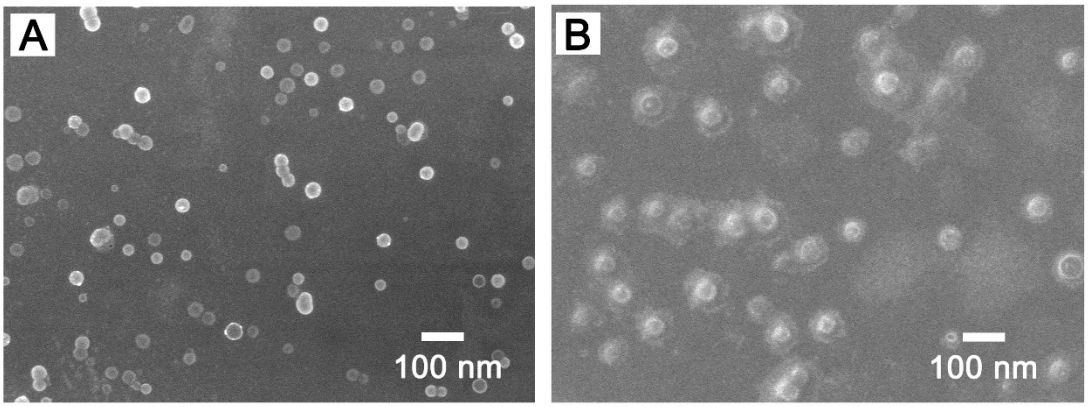

Fig. S14 SEM of (A) PGOHMA and (B) PGOHMA/DNA at N/P = 10.

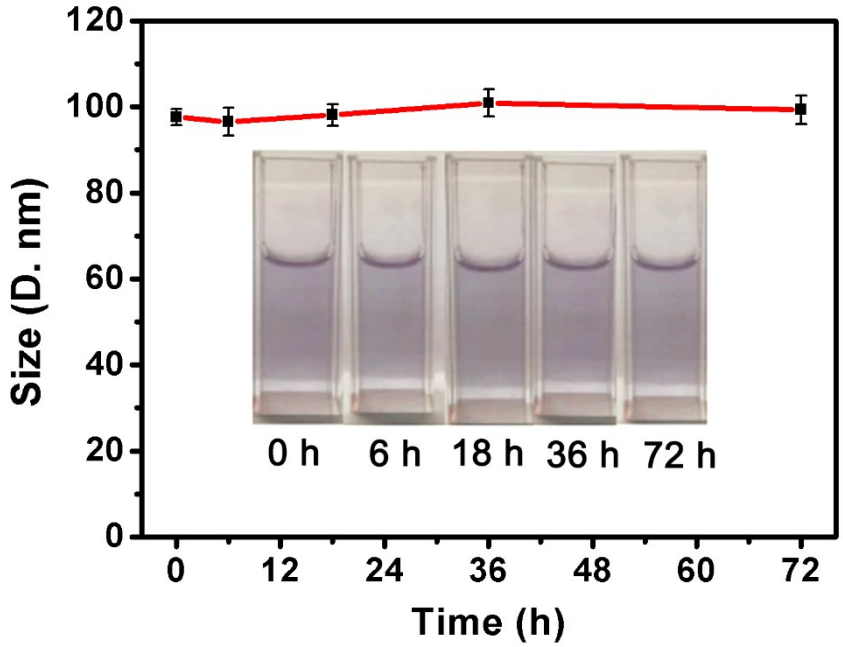

Fig. S15 Size stability of PGOHMA/DNA at N/P = 10.

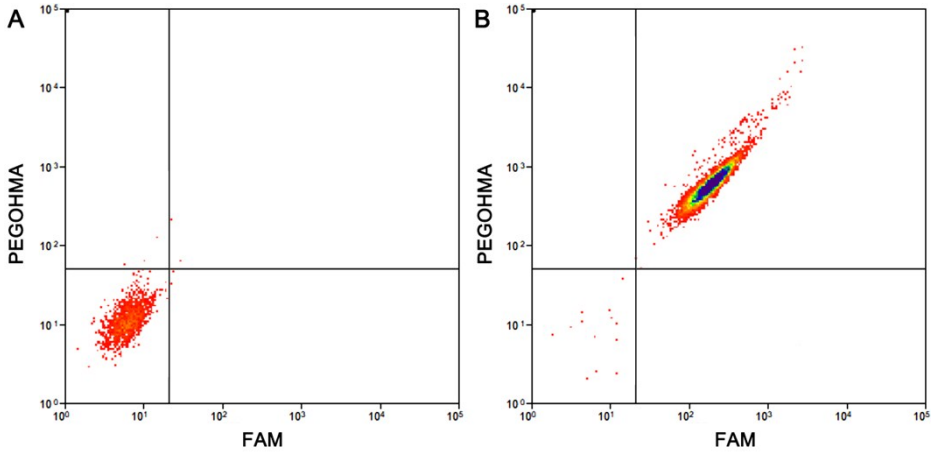

Fig. S16 Flow cytometry analysis of (A) blank (B) and PGOHMA/DNA at N/P = 8.

References

(1) Welsh, D. J.; Jones, S. P.; Smith, D. K. "On - Off" Multivalent Recognition: Degradable Dendrons for Temporary High - Affinity DNA Binding. *Angew. Chem., Int. Ed.* **2009,** *48* (22), 4047-4051.

(2) Gillies, E. R.; Fréchet, J. M. Designing Macromolecules for Therapeutic Applications: Polyester Dendrimer Poly (Ethylene Oxide) "Bow-Tie" Hybrids with Tunable Molecular Weight and Architecture. *J. Am. Chem. Soc.* **2002,** *124* (47), 14137-14146.

(3) Klok, H. A.; Becker, S.; Schuch, F.; Pakula, T.; Müllen, K. Synthesis and Solid State Properties of Novel Fluorescent Polyester Star Polymers. *Macromol. Biosci.*

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