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(oxy methyl) 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$_2$Cl$_2$ and cooled to 0°C. The solution of 2 (1.06 g, 3.2 mmol) in dry CH$_2$Cl$_2$ 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$_2$Cl$_2$ 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$_2$Cl$_2$/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$_2$SO$_4$ (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$_4$OH 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$_2$Cl$_2$ (20 mL) and triethylamine (0.73 mL) at 0 °C. 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. $^1$H NMR (400 MHz, CDCl$_3$, 25 °C): $\delta$= 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, 8 H, -CH$_2$COO), 4.38 (d, 4 H, -CH$_2$-OOC), 4.36 (d, 4 H, -CH$_2$-OOC), 4.34 (t, 8 H, Ph-CH$_2$-), 2.96 (t, 8 H, -CH$_2$-OOC), 2.69 (t, 4 H, Ph-CH-(CH$_3$)$_2$), 1.91 (s, 48 H, -CH$_3$ isobutyrate), 1.32 (s, 12 H, -CH$_3$), 1.12 (d, 24 H, -CH$_3$ isopropyl). $^{13}$C NMR (600 MHz, CDCl$_3$, 25 °C): $\delta$= 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


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