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Supporting Information

Photodegradable Self-Assembling PAMAM Dendrons for Gene Delivery Involving Dendriplexes Formation and Phototriggered Circular DNA Release

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Synthesis of compound 1



4-(benzyloxy)-3-methoxybenzaldehyde b

To a dimethylsulfoxide solution (DMSO, 60 mL) of vanillin *a* (8.50 g, 55.8 mmol) and K₂CO₃ (3.86 g, 27.9 mmol), benzyl chloride (12.8 g, 101 mmol) was added dropwise under N₂. After stirred at 90 °C for 15 h until the disappearance of vanillin, the mixture was cooled to room temperature and then poured into water (100 mL). The organic phase was extracted by ethyl acetate, and rotatory evaporation to dryness afforded the crude product. Recrystallization from ethanol yields compound *b* as white solids (12.3 g, 91%). ¹H-NMR (400 MHz, CDCl₃): δ = 9.83 (s, 1H), 7.30-7.45 (m, 7H), 6.99 (d, *J* = 8.2 Hz, 1H), 5.25 (s, 2H), 3.95 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃): δ = 191.1, 153.8, 150.3, 136.2, 130.5, 128.9, 128.4, 127.4, 126.8, 112.6, 109.6, 71.1, 56.3.

4-(benzyloxy)-5-methoxy-2-nitrobenzaldehyde c

Compound b (5.67 g, 23.4 mmol) was dissvoled in acetic acid (70 mL), followed by adding 65% of nitric acid (10.5 mL) dropwisely under ice bath. The reaction mixture was then stirred

at room temperature for overnigh. The mixture was poured into crused ice, and the nitrified product was extracted by ethyl acetate for 3 times. Combined organic phase was dried over anhydrous magnesium sulfate, and rotatory evaporation to dryness afforded crude compound. Flash column chromatography (SiO₂, ethyl acetate/hexane 3:7) yields compound *c* as yellow solids as yellow solids (5.11 g, 76%). ¹H-NMR (400 MHz, CDCl₃): $\delta = 10.44$ (s, 1H), 7.67 (s, 1H), 7.30-7.47 (m, 6H), 5.27 (s, 2H), 4.02 (s, 3H).

4-hydroxy-5-methoxy-2-nitrobenzaldehyde d

A trifluoroacetic acid solution (TFA, 25 mL) of compound *c* (2.29 g, 7.97 mmol) was stirred at room temperature for overnight under N₂. The volatile was removed under vacuum, and the crude product was rinsed with hexane until complete removal of TFA. Compound *d* was then obtained as pale-yellow solids (1.26 g, 80%). ¹H-NMR (400 MHz, DMSO-d₆): δ = 10.40 (s, 1H), 7.68 (s, 1H), 7.46 (s, 1H), 4.07 (s, 3H). ¹³C-NMR (75 MHz, DMSO-d₆): δ = 187.9, 151.9, 150.5, 143.5, 124.1, 111.2, 110.0, 55.8.

4-(hydroxymethyl)-2-methoxy-5-nitrophenol 1

A ethanol solution (30 mL) of compound *d* (2.92 g, 14.8 mmol) was slowly added by NaBH₄ (2.80 g, 74.0 mmol), and then the reaction mixture was stirred at room temperature until the disappearance of compound *d*. The reaction was quenched by water (5 mL) under ice bath, and the crude product was extracted by ethyl acetate/brine for 3 times. Combined organic phase was dried over anhydrous magnesium sulfate, and rotatory evaporation to dryness afforded compound *I* as pale-yellow solids (2.86 g, 97%). ¹H-NMR (400 MHz, CD₃OD): δ = 7.59 (s, 1H), 7.35 (s, 1H), 4.92 (s, 2H), 3.98 (s, 3H). ¹³C-NMR (75 MHz, CD₃OD): δ = 152.9, 145.5, 139.5, 131.8, 111.5, 109.7, 61.1, 55.5.



Figure S1. (a) ¹H and (b) ¹³C-NMR spectra of compound *4* in CDCl₃ at 25 °C.





Figure S2. ¹H-NMR spectra of (a) **Chol-** G_1 and (b) **Chol-** IG_1 in CD₃OD at 25 °C. The assigned peaks denote to the protons on the triazole (H₁, H₂) and *o*-nitrobenzyl rings (H_a, H_b, H_{a'}, and H_{b'}), which indicates successful click reaction.



Figure S3. MALDI-TOF-MS spectra of (a) **Chol-G**₁ and (b) **Chol-IG**₁ as the protonated (MH⁺) and sodium adducts (MNa⁺). M denotes to the molecular mass.



Figure S4. UV-Vis absorption spectra of **Chol-** G_1 methanolic solution (a) before and (b) after 365-nm light irradiation and of (c) 4-hydroxy-5-methoxy-2-nitrobenzaldehyde *d*. The peak at 280 nm and red-shifted absorption pattern of (b) is close to the absorption profile of (c), suggesting a successful photolysis reaction.



Figure S5. Particle size analysis for the phosphate buffer solutions (PBS, pH = 7.4) of (a) **Chol-***G*₁ and (b) **Chol-***IG*₁ (100 μ M). The z-averaged size distribution was expressed as mean±standard deviation of three measurements.



Figure S6. Particle size analysis for the DNA-**Chol-** G_1 complexes formed in a phosphate buffer solution at N/P = 2. The z-averaged size distribution was expressed as mean±standard deviation of three measurements.



Figure S7. Zeta potential analysis for plasmid DNA (pEGFP-C1) in aqueous solution. The data was expressed as as mean±standard deviation of three measurements.



Figure S8. Zeta potential analysis for DNA-**Chol-** G_1 complexes formed in a phosphate buffer solution at N/P = 2 (a) before and (b) after 365-nm light irradiation. The data was expressed as as mean±standard deviation of three measurements.