Supporting Information

Self-assembled raspberry-like core/satellite nanoparticles for anti-inflammatory protein delivery

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Synthesis of MV-NP core

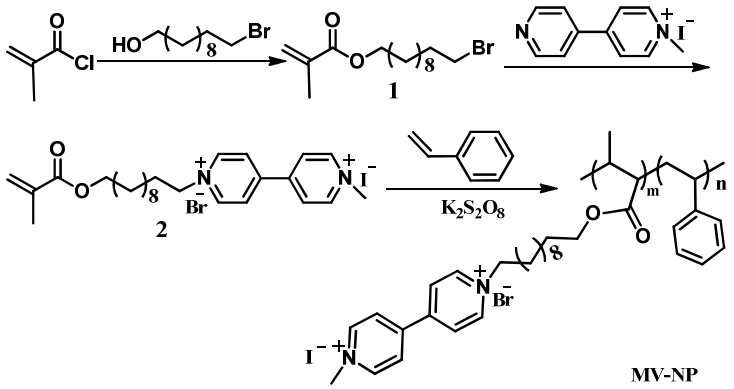

Figure S1. Synthetic routes of **MV-NP**

Synthesis of compound 2.

A mixture solution of compound **1** (450 mg, 1.4 mmol) was dissolved with acetonitrile (20 mL) and then 1-methyl-4,4'-bipyridinium iodide was added 23 (420 mg, 1.4 mmol). The mixture was refluxed with stirring for 36 h and then filtered to get yellow powder in 75% yield. ^{1}H NMR (400 MHz, DMSO): δ 9.41 (d, *J* = 6.6 Hz, 2H), 9.30 (d, *J* = 6.4 Hz, 2H), 8.80 (dd, *J* = 10.4, 6.4 Hz, 4H), 5.98 (s, 1H), 5.64 (s, 1H), 4.69 (t, *J* = 7.4 Hz, 2H), 4.44 (s, 3H), 4.05 (t, *J* = 6.6 Hz, 2H), 1.96 (m, 2H), 1.85 (s, 3H), 1.57 (m, 2H), 1.36-1.17 (m, 14H). ^{13}C NMR (100 MHz, DMSO): δ 166.9, 148.9, 148.5, 147.0, 146.2, 136.4, 127.0, 126.5, 125.9, 64.7, 61.2, 48.4, 31.2, 29.2, 29.2, 29.0, 28.8, 28.4, 25.9, 25.8, 18.4. LC-MS (m/z): $C_{26}H_{38}N_2O_2^{2+}$, calcd, 410.59; found, 410.52.

Synthesis of MV-NP.

The core-shell microspheres of MV-NP were synthesized by the one-stage soap-free emulsion polymerization method according to literature. Briefly, 129 mg of styrene, 200 mg of compound 2, and 20 mL of water were added into a flask and stirred vigorously at room temperature. Subsequently, 13.7 mg of $K_2S_2O_8$ was added and the pH of the dispersion was adjusted to 4 with 0.1 mol/L HCl aqueous solution. The mixture was degassed under nitrogen purge and maintained at 80 ℃ for 24 h under nitrogen atmosphere. After 24 h polymerization, the resultant colloidal dispersion was firstly precipitated in excessive volume of 0.1 mol/L NaOH aqueous solution and then the precipitate was washed with water for three times and dried for further use.

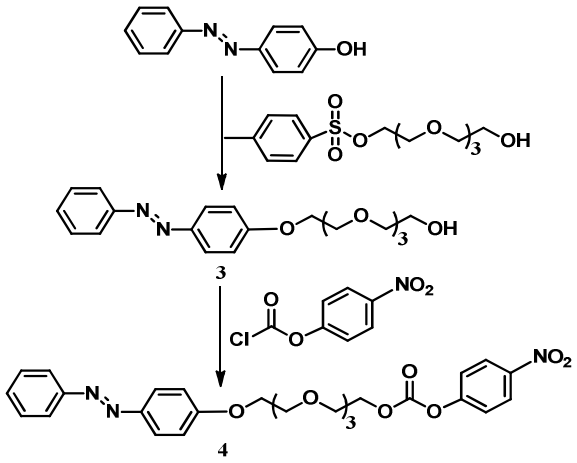

Figure S2. Synthetic routes of compound **4**

Synthesis of compound 4

Compound **3** (630 mg, 1.68 mmol) was dissolved in anhydrous DCM, the reaction was then cooled to 0°C and triethylamine (480 μL) was added. Then 4-Nitrophenyl carbonochloridate (508mg, 2.53 mmol) in DCM (20 mL) was drop added. The reaction mixture was left to stir overnight at room temperature. Water was added and the organic layer was extracted, dried with $MgSO_4$ and evaporated. The crude product was loaded onto a silica gel column and eluted with a 1:10 ethyl acetate/hexane mixture to afford 779 mg (86%) of the product as yellow oil. ^{1}H NMR (400 MHz,$CDCl_3$) δ 8.25 (d, J = 9.0 Hz, 2H), 7.94-7.79 (m, 4H), 7.54-7.45 (m, 2H), 7.48 -7.39 (m, 1H), 7.37 (d, J = 9.0 Hz, 2H), 7.02 (d, J = 8.8 Hz, 2H), 4.46 - 4.39 (m, 2H), 4.22 (t, J = 4.8 Hz, 2H), 3.90 (dd, J = 5.6, 4.0 Hz, 2H), 3.84 - 3.77

(m, 2H), 3.76 (dd, J = 6.4, 3.4 Hz, 2H), 3.71 (d, J = 6.4 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2 , 155.5 , 152.7 , 152.4 , 147.1 ,145.4, 130.4 , 129.0 , 125.3 , 124.7 , 122.5 , 121.7 , 114.8 , 70.9 , 70.7, 70.6, 69.6 , 68.6 , 68.3 , 67.7 . HRMS (ESI): calcd for $C_{27}H_{29}N_3O_9Na^+$ [M+Na^+] 562.1795, found 562.1796.