Supplementary Data

Synthesis of G1-SS-G1

Cystamine dihydrochloride (160 mg, 0.72 mmol) was suspended in EtOAc (15 ml). Triethylamine (0.21 ml, 1.52 mmol) was added, followed by first generation dendritic branch (0.53 g, 1.52 mmol). The reaction mixture was stirred under N_2 for 3 minutes before being cooled to 0°C. DCC (310 mg, 1.52 mmol) and HOBt (206 mg, 1.52 mmol) were added simultaneously as a mixture of solids. The reaction mixture was allowed to warm to room temperature and was stirred for 48 h. The precipitate was removed via filtration. The filtrate was washed with an aqueous saturated solution of sodium hydrogen carbonate, aqueous sodium hydrogen sulfate (8 g in 50 ml), then washed again with aqueous sodium hydrogen carbonate and finally water and brine. The solution was dried over sodium sulfate then rotary evaporated to produce a pale yellow solid (491 mg, 83 %). No further purification was required. R_f 0.54 (CH_2Cl_2:MeOH 90:10), Melting point: 88-90°C; α_D^{293} +18.9 (c = 1.0, $CHCl_3$), +19.23 (c = 1.0, MeOH); *m/z* (ES+) $C_{36}H_{68}N_6O_{10}S_2$ $[M]^+$ requires 808.3; found 831.3 (100%, $[M+Na]^+$); HR FAB-MS calculated for $C_{36}H_{68}N_6O_{10}Na_1S_2$ 831.4336; found 831.4338; δ_H (270 MHz, CD_3OCD_3) 7.70 (2H, t, J 7.5, CON*H*), 6.15 (2H, t, J 8.0, CON*H*), 5.98 (2H, t, J 7.5, CON*H*), 4.10-4.08 (2H, m, COC*H*), 3.54-3.51 (4H, m, SCH_2CH_2NH), 3.06 (4H, q, J 6.5, CH_2CH_2NH), 2.86 (4H, t, J 6.5, SCH_2CH_2NH), 1.9-1.37 (48H, m, CH_2, CH_3); δ_C (67.9 MHz, D_2O) 173.4 (NH*C*OCH x 2), 156.6 (NH*C*OO x 2), 156.3 (NH*C*OO x 2), 79.1 ($OC(CH_3)_3$ x 2), 78.2 ($OC(CH_3)_3$ x 2), 55.3 (NHCO*C*H x 2), 40.6 (SCH_2CH_2NH x 2), 38.9 (CH_2CH_2NH x 2), 38.3 (SCH_2CH_2NH x 2), 33.0 (CH_2 x 4), 28.5 (CCH_3 x 6), 28.4 (CCH_3 x 6), 23.5 (CH_2 x 2); ν_{max} (KBr disc) 3346m (CONH),

2978m, 2935m, 2863w (CH_2, CH_3), 1687s (CONH), 1656s (CONH), 1524s (CONH), 1366m ($C(CH_3)$).

Synthesis of G2-SS-G2

Cystamine dihydrochloride (13 mg, 0.06 mmol) was suspended in EtOAc (5 ml). Triethylamine (18 µl, 0.12 mmol) was added, followed by the second generation dendritic branch (100 mg, 0.12 mmol). The reaction mixture was stirred under N_2 for 3 minutes before being cooled to 0°C. DCC (25 mg, 0.12 mmol) and HOBt (17 mg, 0.12 mmol) were added simultaneously as a mixture of solids. The reaction mixture was allowed to warm to room temperature and was stirred for 4 days. The precipitate was removed via filtration. The filtrate was then washed with an aqueous saturated solution of sodium hydrogen carbonate, aqueous sodium hydrogen sulfate (8 g in 50 ml), then washed again with aqueous sodium hydrogen carbonate and finally water and brine. The solution was dried over sodium sulfate then rotary evaporated to produce 130 mg of a yellow/white solid. The resulting solid was purified using preparative GPC (CH_2Cl_2:MeOH, 90:10) to yield a white solid (40 mg, 39 %). R_f 0.42 (CH_2Cl_2:MeOH 90:10); Melting point: 120-122°C; α_D^{293} +23.3 (c = 1.0, $CHCl_3$), +20.3 (c = 1.0, MeOH); *m/z* (ES+) $C_{80}H_{148}N_{14}O_{22}S_2$ [M]+ requires 1720.7; found 1743.7 (100%, $[M+Na]^+$), 883.6 (12%, $[M+2Na]^{2+}$); δ_H (270 MHz, $CDCl_3$) 7.65 (2H, br s, CON*H*), 7.42 (4H, br s, CON*H*), 5.86 (2H, br s, N*H*Boc), 5.70 (2H, br s, N*H*Boc), 5.06 (2H, br s, N*H*Boc), 4.98 (2H, br s, N*H*Boc), 4.50-4.23 (6H, br m, COC*H*(R)NH), 3.60-3.52 (4H, br m, SCH_2CH_2NH), 3.32-3.30 (4H, br m, CH_2CH_2NH), 3.10-3.05 (8H, br m, CH_2CH_2NH), 2.80-2.75 (4H, br m, SCH_2CH_2NH), 1.79-1.16 (108H, br m, CH_2, CH_3), δ_C (67.9 MHz, $CDCl_3$) 173.6 (*C*ONH x 4), 172.7 (*C*ONH x 2), 156.6

(NH*C*OC(Me)$_3$ x 8), 80.1 (O*C*(Me)$_3$ x 4), 79.2 (O*C*(Me)$_3$ x 4), 54.4 (CO*C*H(R)NH x 4), 54.2 (CO*C*H(R)NH x 2), 40.3 (CH$_2$*C*H$_2$NH x 4), 39.2 (CH$_2$*C*H$_2$NH x 2), 38.8 (CH$_2$*C*H$_2$NH x 2), 38.7 (S*C*H$_2$CH$_2$ x 2), 29.8(*C*H$_2$ x 6), 28.8 (C*C*H$_3$ x 24), 23.1 (*C*H$_2$ x 6), 23.0 (*C*H$_2$ x 6); ν_{max} (KBr disc) 3297m (CONH), 2978m, 2935m (CH$_2$, CH$_3$), 2865w (CH), 1690s (OCONH), 1655s (CONH), 1523s (CONH), 1458w (CH$_2$, CH$_3$), 1366m (C(CH$_3$)$_3$), 1250m, 1715s (COO).

Synthesis of G3-SS-G3

Cystamine dihydrochloride (31 mg, 0.13 mmol) was suspended in EtOAc (5 ml). Triethylamine (40 µl, 0.29 mmol) was added, followed by the third generation dendritic branch (500 mg, 0.29 mmol). The reaction mixture was stirred under N_2 for 3 minutes before being cooled to 0°C. DCC (60 mg, 0.29 mmol) and HOBt (39 mg, 0.29 mmol) were added simultaneously as a mixture of solids. The reaction mixture was allowed to warm to room temperature and was stirred for 4 days. The precipitate was removed via filtration. The filtrate was then washed with an aqueous saturated solution of sodium hydrogen carbonate, aqueous sodium hydrogen sulfate (8 g in 50 ml), then washed again with aqueous sodium hydrogen carbonate and finally water and brine. The solution was dried over sodium sulfate then rotary evaporated to produce 200 mg of a yellow/white solid. The resulting solid was purified using preparative GPC (CH_2Cl_2:MeOH, 90:10) to yield a white solid (160 mg, 34 %). R_f 0.30 (CH_2Cl_2:MeOH 90:10); Melting point: 119-121°C; α_D^{293} –14.4 (c = 1.0, MeOH); *m/z* (ES+) $C_{168}H_{308}N_{30}O_{46}S_2$ [M]+ requires 3548.4; found 1797.1 (100%, $[M+2Na]^{2+}$), 1205.4 (55 %, $[M+3Na]^{3+}$); δ_H (270 MHz, CD_3OD) 4.29 (6H, m, COC*H*(R)NH), 4.00 (8H, m, COC*H*(R)NH), 3.49 (4H, m, SCH$_2$C*H*$_2$NH), 3.18 (12H, m, CH$_2$C*H*$_2$NH), 3.03

(16H, m, CH_2CH_2NH), 2.84 (4H, m, SCH_2CH_2NH), 1.80-1.30 (228H, m, CH_2, CH_3); δ_C (67.9 MHz, CD_3OD) 175.2, 175.0, 172.2, 174.0 (*C*ONH x 14), 158.5 ($NHCOOC(Me)_3$ x 12), 157.8 ($NHCOOC(Me)_3$ x 4), 80.6 ($OC(Me)_3$ x 4), 80.5 ($OC(Me)_3$ x 4), 79.8 ($OC(Me)_3$ x 8), 56.3, 56.2, 54.8, 54.7, 54.6 (All CO*C*H(R)NH x 14), 41.0 (CH_2CH_2NH x 8 and SCH_2CH_2NH x 2), 40.1 (CH_2NH x 6 and SCH_2CH_2NH x 2), 33.3, 32.9, 32.8, 32.6, 30.6, 30.0 (All CH_2), 28.9 (CH_3 x 48), 24.2 (CH_2); ν_{max} (KBr disc) 3310m (CONH), 2977m, 2935m (CH_2, CH_3), 2866w (CH), 1691s (CONH), 1655s (CONH), 1523 s (CONH), 1458w (CH_2, CH_3), 1366m ($C(Me)_3$), 1250m (COO), 1172m (COO).