Supporting Information for

Entropy-Driven Lectin-Recognition of Multivalent Glycovesicles

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Synthesis of 2-[2-[2-(octadecyloxy)ethoxy]ethoxy]ethyl α-D-Manno-pyranoside, tetraacetate: $BF_3.Et_2O$ (360 mg, 2.56 mmol) was added dropwise to a solution of Triethyleneglycolmonooctadecylether (78 mg, 0.18 mmol) and penta-O-acetylmannopyranoside(50 mg, 0.128 mmol) in 3ml of dry dichloromethane by stirring at 0°C.The mixture was allowed to warm to RT and then stirred for a further 48 hrs.The mixture was then poured into $NaHCO_3$ (10ml) and extracted with CH_2Cl_2(3x5)ml. The solvent was evaporated off and the residue was then purified by column chromatography using Hexane/EtOAc (19/1→7:3). The final product appeared as a white wax. ^{1}H NMR(300MHz, $CDCl_3$): δ 0.89 (t, J=6.6 Hz, 3H, CH_3), 1.27 (bs, 30H, CH_2), 1.56 (m, 2H, CH_2), 2.00, 2.06, 2.12, 2.16 (4s, 12H, $4CH_3CO$), 3.46 (tr, J=6.6 Hz, 2H, CH_2) 3.6-3.9(m, 12H, $3CH_2O$), 4.04-4.13 (m, 2H, H-5,H-6'), 4.3 (dd, J= 12.3, 5.1 Hz, 1H,H-6), 4.88 (d, J= 1.5 Hz, 1H, H-1), 5.27 (m, 2H, H-4, H-3), 5.36 (dd, J=10 Hz, 3.5 Hz, 1H, H-2).

*Synthesis of 2-[2-[2-(octadecyloxy)ethoxy]ethoxy]ethyl α-D-Manno-pyranoside,**3***: The acetate protected product (50 mg) was dissolved in dry MeOH/$CHCl_3$(2:1 ml) and 5 mg of MeONa was added. The mixture was stirred at room temperature for 24 hrs. The resulting mixture was neutralised with acidic ion exchange resin and filtered off to yield the desired product. ^{1}HNMR(300MHz, $CDCl_3$, ppm) δ 0.91(t, J=6.6 Hz, 3H, CH_3), 1.29 (bs, 30H, CH_2), 1.58 (m, 2H, CH_2), 3.46 (t, J=6.6 Hz, 2H, CH_2), 3.6-3.9 (m, 15H), 3.82 (m, 2H), 4.3 (dd, J = 12.3, 5.1 Hz, 1H, H-6), 4.80 (d, J=2 Hz, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 12.58(CH_3), 13.5, 21.84, 25.32, 28.58, 28.71, 28.82, 28.88, 31.18, 56.4(CH_2), 60.96(C-6), 65.91(C-4), 66.69, 69.24, 69.51, 69.68, 69.71, 70.2(6CH_2O), 70.52(C-3), 70.65(C-2), 72.66(C-5), 99.85(C-1).

Synthesis of 3',6'-dioxaoctyl-9'-bromo-α-D-mannopyranoside: $BF_3.Et_2O$ (6.9 g, 56 mmol) was added dropwise to a solution of Triethyleneglycol (2.92 mg, 21 mmol) and penta-O-acetylmannopyranoside (2,5 g, 7 mmol) in 15ml of dry dichloromethane by stirring at 0°C.The mixture was allowed to warm to RT and then stirred overnight.The mixture was then washed with $NaHCO_3$ (2x10ml), water (2x10ml) and brine (10ml). After drying with Na_2SO_4, the solvent was evaporated off and the residue was purified by column chromatography using petroleum ether/Et_2O (6:4). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 3.55-3.68 (m, 12H, 6CH_2O), 4.05-4.11 (m, 1H, H-6a), 4.17-4.24 (m, 2H, H-5, H-6b), 5.18 (d, 1H, J_{1-2} = 1.8 Hz, H-1), 5.20 (dd, 1H, J_{2-1} = 1.9 Hz, J_{2-3} = 3.2 Hz, H-2), 5.25 (t, 1H, J_{4-3} = J_{4-5} = 9.9 Hz, H-4), 5.36 (dd, 1H, J_{3-2} = 3,3 Hz, J_{3-4} = 10,1 Hz, H-3); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 20.5-20.7(4CH_3CO), 61.03(C-8'), 62.5(C-6), 66.0(C-4), 66.53(C-1'), 68.1(C-5), 68.8(C-3), 69.94(C-4', C-5'), 70.1(C-2), 70.44(C-2'), 72.60(C-7'), 91.8(C-1), 169.8, 170.1, 170.2, 170.9(4$COCH_3$).

The acetate protected product (2.4 g, 5 mmoles) was dissolved in dry CH_2Cl_2(15 ml) and MeONa (1.6 mg, 50 mmoles) was added. The mixture was stirred at room temperature for 2 hrs. The resulting mixture was neutralised with acidic ion exchange resin and filtered off to yield the desired product. The compound was solubilised in dry tetrahydrofurane (100 ml) in the presence of tetrabromomethane (3.3 g, 10 mmoles). Triphenylphosphine is (2.6 g, 10 mmoles) was then added. The resulting mixture was stirred at room temperature for 10 hrs, then the solvent was evaporated off and the residue was purified by column chromatography using CH_2Cl_2/MeOH (99:1→92:8). ^{1}H NMR (400 MHz, CD_3OD, ppm) δ 3.55-3.67 (m, 12H, 6CH_2O), 4.08-4.13 (m, 1H, H-6a), 4.20-4.27 (m, 2H, H-5, H-6b), 5.22 (d, 1H, H-1), 5.28 (dd, 1H, H-2), 5.25 (t, 1H, H-4), 5.36 (dd, 1H, H-3).).

Synthesis of 8-citrylidene phloroglucinyl-3,6-dioxaoctanyl-α-D-Manno-pyranoside, ***4*** : A solution of citrylidene phloroglucinyl (0.26 g, 1 mmole) and dry cesium carbonate (0.98 g, 3 mmoles) in dry dimethylformamide (5 ml) was stirred for 1 hr at 70°C. Then the brominated compound (0.75g, 2 mmoles) in dry dimethylformamide (5 ml) was added and the mixture was stirred for 3 hrs at 50°C. Then the mixture was poured into saturated NaCl solution, extracted with CH_2Cl_2 (3x5)ml and dried with Na_2SO_4, the solvent was evaporated off and the residue was purified by column chromatography. The product was obtained as a white powder. ^{1}H NMR(400MHz, $CDCl_3$, ppm) δ 4.09-4.21 (m, 2H, H-6), 5.22 (d, 1H, H-1), 5.31 (dd, 1H, H-2), 5.26 (t, 1H, H-4), 5.41 (dd, 1H, H-3), 3.71-3.58 (12H, m, 6CH_2O), 6.04 (2H, s, H-2', H-4'), 2.84 (1H, ddd, H-9'), 2.23 (1H, ddd, H-8'a), 2.03 (1H, ddd, H-12'), 1.83 (1H, dd, H-8'b), 1.74 (1H, ddd, H-10'a), 1.54 (3H, s, H-14'), 1.45 (1H, dt, H-10'b), 1.39 (3H, s, H-16'), 1.28 (3H, d, H-6'), 1.24 (1H, dt, H-11'a), 1.05 (3H, s, H-15'), 0.69 (1H, dddd, H-11'b) ; ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 159.2(C-3'), 157.9(C-5'), 157.5(C-1'), 110.1(C-6'), 100.3(C-1), 98.3(C-4'), 98.2(C-2'), 84.6(C-7'), 75.3(C-13'), 73.4(C-4), 72.1(C-3), 71.3(C-2), 71.2, 70.9, 70.6, 70.1(4CH_2O), 68.5(C-5), 68.0(CH_2O), 66.9(CH_2O), 47.1(C-12'), 37.7(C-10'), 35.7(C-8'), 30.1(C-14'), 29.4(C-16'), 28.2(C-9'), 24.2(C-15'), 22.4(C-11'), 60.0(C-6).

1.5 mg of POPC was dissolved in iso-propanol (50 µl). This solution was then injected into 1 ml of Buffer (PBS or Tris) (pH 7.4) (NaCl 100 mM) with rapid shaking on a "paramix II" shaker for one minute resulting in a clear solution. This solution was then ultrasonicated for 30 minutes at 0°C before being diluted (x10) with buffer giving a final concentration of 200 µM in POPC.

The starting vesicle composition was POPC : POPG (80 : 20). The mannoside ligand (3,4) were incorporated at different ratios (0 to 30 % w:w to phospholipids POPC:POPG:**3,4** (77.5:17.5:**5** to 65:5:**30**). Then 2 ml of $CHCl_3$/MeOH were added to each sample. After manual stirring the solutions were evaporated and dried under vacuum during at least 4 hrs leading to the formation of a lipid film. The different lipid mixtures were then hydrated using 200 microL of PBS (100 mM, pH 7.4). The lipid suspension should be kept above the phase transition temperature of the lipids during hydration and extrusion. The hydrated lipid suspension was subjected to 7 freeze/thaw cycles by alternately placing the sample vial in a liquid nitrogen bath and allowing it to return to room temperature. Extrusion of the multilamellar liposomal suspensions was performed using membranes with a pore size of 100 nm. Two additionnal filters were added on either side of the membrane to prevent the occurrence of any damage. The solutions were passed 29 times through the membrane. The

lipid suspension begins to clarify to yield a slightly hazy transparent solution. The LUVs solution was then tested of their lectin specificity by continuous flow QCM analysis