'Multicopy Multivalent' Glycopolymer-stabilised Gold Nanoparticles as Potential Synthetic Cancer Vaccines – Supporting Information

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General Experimental Details

All chemicals were used without further purification unless stated otherwise. Ceric ammonium nitrate (CAN) (>98 %), sodium azide, diisopropylethylamine (DIPEA) (>99 %), trichloroacetonitrile (98 %), 2-hydroxyethyl methacrylate (99+ %), acetic anhydride, 4-(N,N-dimethylamino)pyridine (DMAP) (99+ %), sodium borohydride (> 98 %), potassium carbonate, poly(ethylene glycol) methyl ether methacrylate (M_n = 300; PEGMA), 4,4`-azobis(4-cyanovaleric acid) (ACVA) and bovine submaxillary mucin (BSM) were purchased from Sigma Aldrich. 3,4,6-Tri-*O*-acetyl galactal (99 %) was purchased from Carbosynth. Thiophenol (> 99 %) was purchased from Fluka. 1,2-bis(diphenylphosphino)ethanetriphenylphosphine (DPPE) and hydrogen tetra-chloroaurate (> 99.9 %, 49 % Au by mass) were purchased from Alfa Aesar. Solvents were purchased from Fischer Scientific and dried by passage through two alumina columns using an Innovative Technology Inc. solvent purification system and stored under N_2. TLC was performed on aluminium-backed silica plates (Merck), with visualisation using H_2SO_4 (5 %) in ethanol. 2-Hydroxyethyl methacrylate was passed through a short column of basic alumina in order to remove MEHQ inhibitor prior to polymerisation. Flash column chromatography was performed using a Biotage SP1 automated purification system using pre-packed silica columns. (4-cyanopentanoic acid)-4-dithiobenzoate (CPADB) was synthesised according to a previously described procedure[1]; analytical data were in agreement with literature values.

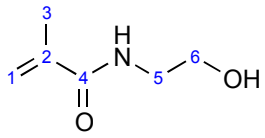
Instrumentation

NMR spectra were recorded on a Varian Inova-700 spectrometer at 700MHz (^{1}H) and 176MHz (^{13}C), a Varian Inova 500 spectrometer at 499.87 (^{1}H) and 125.67 MHz (^{13}C, ^{1}H decoupled at 500 MHz) or a Bruker Avance 400 spectrometer at 400.13 MHz (^{1}H) or 100.26 MHz (^{13}C, ^{1}H decoupled at 400 MHz), at ambient temperature in $CDCl_3$, DMSO, D_2O or MeOD. NMR spectra were analysed using MestReNova v6.04 software and referenced internally to the protons of the residual solvent. IR spectra were recorded on a Nicolet Nexus FT-IR spectrometer as thin films on KBr discs cast from a suitable solvent. Mass spectral analyses were performed on a Thermal-Finnigan LTQ using a positive or negative ionisation electrospray mode. Elemental analysis was conducted on an Exeter Analytical E-440 elemental analyser. SEC was performed using a triple detection method (with angular correction) and measurements were performed on a Viscotek TDA 301 triple detection SEC fitted with two (300 x 7.5 mm) GMPWxl methacrylate-based mixed bed columns with an exclusion limit of 5,107 g mol^{-1}, having refractive index, viscometer and RALLS detectors. The eluent was DMF with added LiBr salt at a flow rate of 1.0 ml min^{-1}. Thermogravimetric analyses were performed on a Perkin Elmer Pyris 1 TGA under argon gas; heating from 20 °C to 800 °C at 10 °C min^{-1}. Dynamic light scattering measurements were acquired using a Brookhaven Instruments 90 Zeta-Plus particle size analyser; samples were passed through a 0.22 μm

syringe filter prior to analysis. Samples for TEM analysis were prepared by deposition of a drop of the particle solution on to a carbon-coated copper grid and the excess solution removed using filter paper, leaving a thin film of the particles. The samples were imaged using a Hitachi H7600 microscope.

Synthetic Procedures

N-(2-Hydroxyethyl)-2-methacrylamide (HEMAm)



N-(2-hydroxyethyl)-2-methacrylamide (HEMAm) was prepared according to the method described by Chan et al.[2] Freshly distilled methacryloyl chloride (1.30 cm^3, 13.4 mmol) was dissolved in anhydrous dry chloroform (15 cm^3) and added slowly to a solution of ethanolamine (1.62 cm^3 , 26.8 mmol) at 0 °C in anhydrous chloroform (20 cm^3). The reaction was stirred for a further 2 h at 0 °C, after which the precipitated salt was removed by filtration, and the solvent removed *in vacuo* to yield crude HEMAm as a colourless oil. This was dissolved in chloroform and stirred overnight with basic alumina. After filtration, the solvent was removed *in vacuo* to give the final product as a pale yellow oil, which was stored with BHT at ~4 °C in order to prevent unwanted polymerisation (1.50 g, 11.4 mmol, 90 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.25 (s, 1H, NH), 5.68 (s, 1H, H-1, E to CH_3-C=C), 5.35 (s, 1H, H-1, Z to CH_3-C=C), 3.73–3.69 (m, 2H, H-5), 3.43 (dd, J = 5.5Hz, 10.2Hz, 2H, H-6), 2.70 (s, 2H, H-3). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.70 (C-4), 140.06 (C-2), 119.37 (C-1), 62.20 (C-6), 39.44 (C-5), 18.64 (C-3). LR-MS (ES+) m/z requires 152.1, found 152.1 $(M+Na)^+$.

3,4,5-Tri-*O*-Acetyl-2-Azido-2-Deoxygalactopyranosyl Nitrate

A solution of tri-*O*-acetyl galactal (12.0 g, 44 mmol) in acetonitrile (250 cm^3) was cooled to 0 °C and transferred by cannula into a cooled (-20 °C) mixture of NaN_3 (4.3 g, 66 mmol) and ceric ammonium nitrate (87 g, 158 mmol). The reaction mixture was vigorously stirred under N_2 at -20 °C for 12 h. Upon reaction completion as determined by TLC, the mixture was diluted with ethyl acetate (150 cm^3), and washed with cold water (5 x 50 cm^3) and brine subsequently. The solution was dried over anhydrous Na_2SO_4, filtered and the solvent removed *in vacuo*. The colourless oil (15.5 g) was purified by flash column chromatography (EtOAc/hexane 1:1). A mixture of α, β and talo stereoisomers was isolated in a ratio of 1:0.7:0.2 (as determined by ^{1}H NMR spectroscopy), (13.3g, 35.3 mmol, 80 %). The individual stereoisomers were not isolated although, for clarity, NMR data for each is reported separately. $\nu_{max}(CH_2Cl_2/cm^{-1})$ 3476, 2959, 2119 (N_3), 1815, 1747, 1660, 1372, 1224 cm^{-1}; **α** ^{1}H NMR (700MHz,

$CDCl_3$): δ 6.36 (d, $J_{1,2}$ = 4.2Hz, 1H, H-1), 5.50 (dd, $J_{4,5}$= 0.7Hz, $J_{4,3}$ = 3.1Hz, 1H, H-4), 5.26 (1H, dd, $J_{3,2}$=11.3Hz, $J_{3,4}$=3.1Hz, 1H, H-3), 4.14 (m, 1H, H-2), 5.24 (dd, $J_{3,2}$ 11.5Hz, $J_{3,4}$ = 2.9Hz, 1H, H-3), 4.37 (td, $J_{5,4}$= 0.7Hz, $J_{5,6}$ = 6.2Hz, 1H H-5), 4.16–4.11 (m, 3H, H-2, H-6), 2.12–2.03 (m, 9H, $3CH_3$); ^{13}C NMR (126MHz, $CDCl_3$): δ 169.4 – 170.3 (C=O acyl), 97.1 (C-1), 69.7 (C-5), 69.0 (C-3), 66.5 (C-4), 61.1 (C-6), 56.3 (C-2), 20.8-20.3 (3 x CH_3); **β** ^{1}H NMR (700MHz, $CDCl_3$): δ 5.60 (d, $J_{1,2}$ = 8.8Hz, 1H, H-1), 5.40 (dd, $J_{4,3}$ = 3.3Hz, $J_{4,5}$= 0.8Hz, 1H, H-4), 4.97 (dd, $J_{3,4}$ = 3.3Hz, $J_{3,2}$ = 10.6Hz, 1H, H-3), 4.15–4.11 (m, 2H, H-6), 4.05 (td, $J_{5,4}$= 0.8Hz, $J_{5,6}$ = 6.6Hz, 1H, H-5), 3.86 (dd, $J_{2,3}$ = 10.6Hz, $J_{1,2}$= 8.8Hz, 1H, H-2), 2.12–2.03 (m, 9H, 3x CH_3); ^{13}C NMR (126MHz, $CDCl_3$): δ 169.4 – 170.5 (C=O) 98.4 (C-1), 72.0 (C-5), 71.9 (C-3), 66.3 (C-4), 60.9 (C-6), 57.7 (C-2), 20.8-20.3 (CH_3); **talo** ^{1}H NMR (500MHz, $CDCl_3$): δ 6.21 (d, $J_{1,2}$ = 1.2Hz, 1H, H-1), 5.48-5.44 (m, 1H, H-4), 5.30 (dd, $J_{3,2}$ = 3.7Hz, $J_{3,4}$ = 4.8Hz, 1H, H-3), 4.19 (td, $J_{5,4}$ =5.4Hz, $J_{5,6}$ =11.8Hz, 1H, H-5), 4.16–4.11 (m, 2H, H-6), 4.01 (1H, m, H-2), 2.12- 2.03 (m, 9H, 3 x CH_3); ^{13}C NMR (126MHz, $CDCl_3$): δ 169.4 – 170.5 (C=O), 97.9 (C-1), 67.4 (C-3), 65.0 (C-4), 61.3 (C-6), 60.7 (C-5), 55.4 (C-2), 20.8-20.3 (3 x CH_3). LRMS (ES+) requires m/z 399.0, found 399.0 $(M+Na)^+$; Anal. calcd. for $C_{12}H_{16}N_4O_{10}$: C 38.30, H 4.29, N 14.55; found: C 38.42, H 4.31, N 14.47.

3,4,5-Tri-*O*-Acetyl-2-Azido-2-Deoxygalactose

A solution of azidonitrates (13g, 35.3mmol) in anhydrous acetonitrile (100 ml) at 0 °C was treated with DIPEA (7.6ml, 42.4mmol) and thiophenol (4.4ml, 42.4mmol). The reaction mixture was stirred at 0 °C for 1 h, after which the solvent was removed *in vacuo.* The dark brown residue was then treated with hexane and the solvent decanted in order to remove a large proportion of the diphenyl disulphide byproduct. The remaining oil was purified by flash column chromatography (EtOAc:hexane 1:1) to give a pale yellow viscous oil (8.2g, 24.7 mmol, 72 %). A mixture of α and β anomers was isolated in a ratio of 0.5:1, as determined by ^{1}H NMR spectroscopy (the talo isomer was separated by column chromatography). The individual anomers were not isolated although, for clarity, NMR data for each is reported separately. $\nu_{max}(CH_2Cl_2/cm^{-1})$ 3642 (OH) 2118 (N_3), 1743 (C=O). **α** ^{1}H NMR (700 MHz, $CDCl_3$): δ 5.45 (dd, $J_{4,5}$ = 1.4Hz, $J_{4,3}$ = 3.3Hz, 1H, H-4), 5.42 (t, $J_{1,OH}$ = 3.4Hz, $J_{1,2}$ = 3.4Hz, 1H, H-1), 5.39 (dd, $J_{3,4}$ = 3.2Hz, $J_{3,2}$ 11.1Hz, 1H, H-3), 4.45 (td, $J_{5,4}$ = 0.9Hz, $J_{5,6}$ 6.5Hz, 1H, H-5), 4.08 (m, 2H, H-6), 3.74 (dd, $J_{2,1}$ = 3.4Hz, $J_{2,3}$ = 11.1Hz, 1H, H-2), 3.17 (d, J_{OH-1} = 3.5Hz, 1H, OH), 2.14-2.04 (m, 9H, 3 x CH_3); ^{13}C NMR (176 MHz, $CDCl_3$): δ 170.4-169.8, (C=O), 92.39 (C-1), 68.30 (C-3), 67.64 (C-4), 66.67 (C-5), 61.74 (C-6), 58.01 (C-2), 20.6-20.5 (3 x CH_3). **β** ^{1}H NMR (700 MHz, $CDCl_3$): 5.33 (dd, $J_{4,5}$ = 1.0, $J_{4,3}$ 3.4, 1H, H-4), 4.81 (dd, $J_{3,4}$ = 3.4, $J_{3,2}$ =10.9, 1H, H-3), 4.70 (dd, $J_{1\text{-}OH}$ = 5.3, $J_{1,2}$ = 7.9, 1H, H-1), 4.12 (d, $J_{6,5}$ = 6.5, 2H, H-6), 3.90 (td, $J_{5,4}$ = 1.2, $J_{5,6}$ = 6.5, 1H, H-5), 3.72 (d, J_{OH-1} = 5.4, 1H, OH), 3.65 (dd, $J_{2,1}$ = 7.9, $J_{2,3}$ = 10.9, 1H, H-2), 2.15-2.04 (m, 9H, 3 x CH_3); ^{13}C NMR (176 MHz, $CDCl_3$): δ 170.4-169.8 (C=O), 96.44 (C-1*)*, 71.14 (C-3), 70.99 (C-5), 66.41 (C-4), 61.97 (C-2), 61.54 (C-6), 20.6-20.5 (CH_3). LR-MS (ES^+) m/z requires 354.2, found 354.0 $(M + Na)^+$.

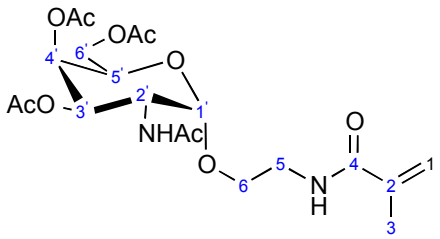
3,4,6-Tri-*O*-Acetyl-2-Azido-2-Deoxy-D-Galactopyranosyl Trichloroacetimidate (1)

3,4,5-Tri-*O*-acetyl-2-azido-2-deoxygalactose (8.1 g, 24.4 mmol) was dissolved in anhydrous dichloromethane (100 cm^3), cooled to 0 °C and treated with K_2CO_3 (17 g, 122.2 mmol) and trichloroacetonitrile (35 cm^3, 244 mmol). The reaction mixture was allowed to warm to room temperature and stirred for 12 h. The suspension was filtered through a pad of Celite and washed with anhydrous dichloromethane. The filtrate was concentrated *in vacuo*, and the dark brown oily residue was purified by flash chromatography on silica gel (EtOAc/hexane 1:1) to give a pale yellow viscous oil (7.6 g, 16.0 mmol, 62 %). A mixture of α and β anomers was isolated in a ratio of 1:1, as determined by ^{1}H NMR spectroscopy. $\nu_{max}(CH_2Cl_2/cm^{-1})$ 3318 (NH), 2962 (sp^3 CH str), 2116 (N_3), 1750 (C=O), 1675 (NHC=O), 1370, 1224, 1071; **1α** ^{1}H NMR (700 MHz, $CDCl_3$): δ 8.78 (s, 1H, NH), 6.50 (d, $J_{1,2}$ = 3.6Hz, 1H, H-1), 5.53 (dd, $J_{4,5}$ = 1.3Hz, $J_{4,3}$ 3.2Hz, 1H, H-4), 5.37, (dd, $J_{3,4}$ =3.2Hz, $J_{3,2}$ = 11.1Hz, 1H, H-3) 4.17–4.10 (m, 3H, H-5,H6), 4.05 (dd, J = 6.7Hz, 11.4Hz, 1H, H-2), 2.16 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 1.99 (s, 3H, CH_3). ^{13}C (176MHz, $CDCl_3$): δ C 169.9–170.5 (C=O), 160.9 (C-7), 96.9 (C-1), 90.8 (C-8), 69.3 (C-5), 68.9 (C-3), 67.2 (C-4), 61.4 (C-6), 57.3 (C-2), 20.8 (CH_3). **1β** ^{1}H NMR (700 MHz, $CDCl_3$): δ 8.78 (s, 1H, NH), 5.69 (d, $J_{1,2}$ = 8.5Hz, 1H, H-1), 5.39 (dd, $J_{4,5}$ = 1.1Hz, $J_{4,3}$ = 3.4Hz, 1H, H-4), 4.90 (dd, $J_{3,4}$ = 3.4Hz, $J_{3,2}$ = 10.8Hz, 1H, H-3), 4.40 (td, $J_{5,4}$ = 1.1Hz, $J_{5,6}$ = 6.6Hz, 1H, H-5), 4.03-4.00 (m, 2H, H-6,6) 3.94 (dd, $J_{2,3}$ = 8.5Hz, $J_{2,1}$ = 10.8Hz, 1H, H-2), 2.17 (s, 3H, CH_3, 2.06 (s, 3H, CH_3), 2.02 (s, 3H, CH_3); ^{13}C NMR (176MHz, $CDCl_3$): δ 169.9–170.5 (C=O), 160.9 (C-7), 94.7 (C-1), 90.5 (C-8),71.9 (C-5), 71.5 (C-3), 66.2 (C-4), 61.0 (C-6), 60.6 (C-2), 20.8 (CH_3). LR-MS (ES^+) m/z requires 497.0, found 497.0 $(M + Na)^+$; Anal. calcd. for $C_{12}H_{17}N_3O_8$: C 35.35, H 3.60, N 11.78; found: C 35.21, H 3.56, N 11.54.

3,4,6-Tri-*O*-Acetyl-2-Azido-2-Deoxy-D-Galactopyranosyloxyethyl Methacrylamide

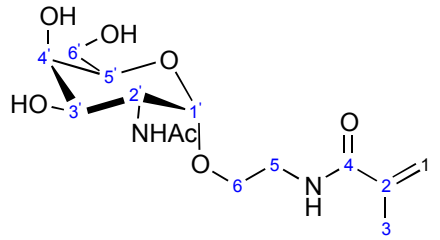
A solution of trichloroacetimidate **1** (5.8 g, 12.1 mmol), HEMAm (1.8 g, 13.9 mmol) with 3 Å molecular sieves in diethyl ether:dichloromethane (2:1), was cooled to -20 °C under N_2. TMSOTf (1.1 cm^3, 6.05 mmol) was added and the reaction stirred for 30 min., after which time **1** had been consumed (as determined by TLC). The reaction was quenched with Et_3N (0.85 cm^3, 6.1 mmol), stirred for a further 15 min., filtered to remove Et_3N.HCl and then concentrated *in vacuo*. The crude product was purified by flash column chromatography (EtOAc:hexanes, 1:1) to give a pale yellow oil (4.3 g, 9.7 mmol, 80 %). A α:β ratio of 1:1 was determined by ^{1}H NMR spectroscopy. HRMS *m/z* $(ES)^+$: Found 465.1589 $(M+Na)^+$. $C_{18}H_{26}N_4NaO_9$ requires *m/z* 465.1592. Anal. calcd. for $C_{18}H_{26}N_4O_9$: C 48.87, H 5.92, N 12.66, found C 49.11, 5.94, N 12.57.

3,4,6-Tri-*O*-Acetyl-2-*N*-Acetamido-2-Deoxy-α-D-Galactopyranosyl-oxyethyl Methacrylamide



To a solution of 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-D-galactopyranosyloxyethyl methacrylamide (4.2 g, 9.5 mmol) in dichloromethane (60 cm^3) was added DPPE (3.0 g, 7.6 mmol). The reaction was stirred for 1 h after which Ac_2O (9 cm^3, 95 mmol), DMAP (0.23g, 1.9 mmol) and Et_3N (19 cm^3, 142.5 mmol) were added. The reaction was stirred for a further 3 h until the intermediate DPPE adduct had been consumed and the product spot appeared by TLC (toluene:acetone, 1:1, R_f 0.33). The reaction mixture was filtered to remove precipitated bis(phosphine oxide) and the solvent then removed *in vacuo*. The crude residue was purified by flash column chromatography (toluene: acetone, 1:1) to give the separate anomers (**α**: 1.91g, 4.2 mmol, 55 %) and (**β**: 1.7g, 3.7 mmol, 40 %) as clear, colourless oils. **α** ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.29 – 6.20 (m, 1H, NH), 6.07 (d, $J_{NH,2'}$ = 8.9Hz, 1H, NHAc), 5.72 (s, 1H, H-1, E to CH_3-C=C), 5.40 (s, 1H, H-1, Z to CH_3-C=C, ov m, 1H, H-4'), 5.15 (dd, $J_{3',4'}$ = 3.3Hz, $J_{3',2'}$ = 11.4Hz, 1H, H-3'), 4.92 (d, $J_{4',3'}$ = 3.6Hz, 1H, H-1'), 4.61 (ddd, $J_{2',1'}$ = 3.6Hz, $J_{2'\text{-NH}}$ = 9.5Hz, $J_{3',2'}$ = 11.4Hz, 1H, H-2'), 4.20 (t, $J_{5',6'}$ = 6.3Hz 1H, H-5') 4.16-4.04 (m, 3H, H-5a, H-6'), 3.79 (ddd, $J_{6a,5b}$ = 4.2Hz, $J_{6a,5a}$ = 6.7Hz, $J_{6a,6b}$ = 8.3Hz, 1H, H-6a), 3.72-3.65 (m, 1H, H-5b), 3.63 – 3.47 (m, 1H, H-6b), 2.19 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 2.01 (s ov, 6H, H-3, NHAc).^{13}C NMR (126 MHz, $CDCl_3$): δ 171.18, 170.73, 170.52, 170.31, 167.42 (5 x C=O), 136.18 (C-2), 126.38 (C-1), 98.04 (C-1'), 68.60 (C-3'), 67.32 (C-5'), 67.15 (C-4'), 65.98 (C-6), 61.23 (C-5), 62.15 (C-6'), 47.78 (C-2'), 23.46 (NHAc), 20.97 (CH_3), 20.89 (CH_3), 20.87 (CH_3), 18.54 (C-3).

2-*N*-Acetamido-2-Deoxy-α-D-Galactopyranosyloxyethyl Methacrylamide (2)



To a stirred solution of 3,4,6-tri-*O*-acetyl-2-*N*-acetamido-2-deoxy-α-D-galactopyranosyloxyethyl methacrylamide (1.0 g, 2.2 mmol) in anhydrous methanol (30 cm^3) was added K_2CO_3 (0.36 g, 2.6 mmol).

The reaction was quenched with cation exchange resin (DOWEX 50W x 2-200) after 20 min. following full deprotection of the sugar as determined by TLC. The neutral solution was stirred for a further 20 min. before filtration through Celite to remove the resin. The solution was concentrated *in vacuo* and the residue then purified by flash column chromatography (CH_3Cl:MeOH, 6:1). The fully deprotected alpha sugar was isolated as a white powder (0.47 g, 1.4 mmol, 65 %). ν_{max}(MeOH/cm^{-1}) 3346, 3016, 2952, 1748, 1721 (C=O HEMA), 1664, 1557. ^{1}H NMR (700 MHz, CD_3OD): δ 5.69 (s, 1H, H-1, E to CH_3-C=C), 5.38 (s, 1H, H-1, Z to CH_3-C=C), 4.79 (d, $J_{1',2'}$ = 3.6Hz, 1H, H-1'), 4.26 (dd, $J_{2',1'}$ = 3.60Hz, $J_{2',3'}$ 10.9Hz, 1H, H-2'), 3.84 (d, $J_{4',3'}$ = 2.9Hz, 1H, H-4'), 3.78 (t, $J_{5',6'}$ = 6.3Hz, 1H, H-5'), 3.76 – 3.69 (m, 3H, H-5a, H-6'), 3.67 (dd, $J_{3',4'}$ = 4.8Hz, $J_{3',2'}$ 11.2Hz, 1H, H-3'), 3.57 (ddd, $J_{6a,5b}$ = 4.5Hz, $J_{6a,5a}$ = 6.5Hz, $J_{6a,6b}$ = 13.6Hz, H, H-6a), 3.52 (ddd, $J_{5b,6a}$ = 4.5Hz, $J_{5b,6b}$ = 6.2Hz, $J_{5b,5a}$ = 10.7Hz, 1H, H-5b), 3.38 (ddd, $J = J_{6b,5a}$ = 4.2Hz, $J_{6b,5b}$ = 5.9Hz, $J_{6b,6a}$ = 13.3Hz, 1H, H-6b), 1.97 (s, 3H, NHAc), 1.94 (s, 3H, H-3). ^{13}C NMR (176 MHz, CD_3OD): δ 172.45 (NHC=O), 170.03 (C-4), 139.97 (C-2), 119.07 (C-1), 97.88 (C-1'), 71.28 (C-5'), 68.95 (C-4'), 68.56 (C-3'), 66.65 (C-6), 61.47 (C-5), 49.98 (C-2'), 38.95, 21.31 (NHAc), 17.36 (C-3). HRMS *m/z* $(ES)^+$: Found 355.1479 $(M+Na)^+$. $C_{14}H_{23}N_2NaO_8$ requires *m/z* 355.1481.

RAFT Polymerisation of Monomer 2

To a solution of **2** ($5.0x10^{-2}$ g, 0.15 mmol) in DMF:H_2O (7:3) (1 cm^3) in a Schlenk tube were added solutions of CPADB (50 µl, 0.057 M, $3.0x10^{-3}$ mmol) and ACVA (26 µl, 0.057 M, $1.5x10^{-3}$ mmol), also in DMF:H_2O (7:3). The tube was sealed and the solution degassed by 5 freeze-pump-thaw cycles, back-filled with N_2 and placed in a water bath at 70 °C. After 24 h a further portion of ACVA was added (13 µl, 0.057 M, $7.5x10^{-4}$ mmol) after which the flask was resealed, purged with N_2 and the reaction heated at 70 °C for another 24 h. The polymerisation was quenched after 48 h by immersion in ice water. A crude sample was taken for ^{1}H NMR analysis and the remainder of the solution was dialyzed against high purity water (3 x 2L) and the purified polymer solution lyophilized to yield a pale pink solid.

Statistical Copolymers of 2 and PEGMA

Table S1: Quantities Used in the Synthesis of Statistical Copolymers of 2 and PEGMA[a]

Sample[b]	PEGMA		[CPADB]		[ACVA]		[M]/ [CTA]	[CTA/ Init.]
	g	mmol	mg	µmol	mg	µmol		
$PEG_{40}Tn_{10}$	0.18	0.60	4.2	15	2.1	7.5	50	2
$PEG_{25}Tn_{25}$	0.045	0.15	1.7	6.0	0.8	3.0	50	2
$PEG_{80}Tn_{20}$	0.18	0.60	2.0	7.5	1.1	3.8	100	2
$PEG_{50}Tn_{50}$	0.045	0.15	0.8	3.0	0.4	1.5	100	2

[a] Quantity of **2** = 0.05g (0.15 mmol) throughout, PEGMA = poly(ethyleneglycol) methyl ether methacrylate, Tn = Tn-antigen glycan monomer **2**, M = monomer, CTA = chain transfer agent (CPADB), Init. = initiator (ACVA); [b] PEG = poly(ethyleneglycol) methyl ether methacrylate, Tn = Tn-antigen glycan monomer **2**, subscript = target degree of polymerization.

Statistical copolymers were synthesised using quantities detailed in Table S1. Typically (entry 1), **2** (0.05 g, 0.15 mmol) and poly(ethyleneglycol) methyl ether methacrylate (PEGMA) (0.18 g, 0.60 mmol) were dissolved in DMF:H_2O (7:3) to give a 0.5M solution. CPADB ($4.2x10^{-3}$ g, 0.015 mmol) and ACVA ($2.1x10^{-3}$, $7.5x10^{-3}$ mmol) were added as solutions in DMF:H_2O (7:3), the mixture degassed by five freeze-pump-thaw cycles and subsequently backfilled with N_2. The flask was placed in a water bath at 70 °C for 24 h. After 24 h a further portion of ACVA was added (13 µl, 0.057 M, $7.5x10^{-4}$ mmol) after which the flask was resealed, purged and the reaction then heated at 70 °C for an additional 24 h. The polymerisation was quenched after 48 h by immersion in ice water. A sample of the solution was removed for ^{1}H NMR analysis of the crude reaction mixture and the remainder was dialysed against high purity water (3 x 2L H_2O) for 24 h. Typical ^{1}H NMR spectroscopy data are as follows (all are identical except for integration values due to differences in composition). ^{1}H NMR (700 MHz, D_2O): δ 7.92-7.18 (br, NH), 4.29-4.14 (br, H-1'), 4.13-3.91 (br, CH_2OCO), 3.85-3.08 (br m, H-H-2'-H-6', H-5, H-6, PEG-CH_2, PEG-OCH_3), 2.05-1.35, (backbone CH_2, NHAc), 1.17-1.05 (backbone CH_3).
Molecular weight and composition data for the polymers are given in Table S2.

Table S2. Data for the Synthesis of Polymers by RAFT Polymerisation

Polymer[a]	Conversion (%)[b]	Yield (%)	$M_{n,\,Th}$ (kDa)[c]	M_n (kDa)[d]	PDI[d]
PEG_{50}	95	51	14.5	12.2	1.23
Tn_{50}	65	52	11.1	14.2	1.16
$PEG_{40}Tn_{10}$	99, 95[e]	73	15.3	15.0	1.12
$PEG_{25}Tn_{25}$	90, 70[e]	59	12.9	16.9	1.18
$PEG_{80}Tn_{20}$	99, 75[e]	68	29.0	40.4	1.15
$PEG_{50}Tn_{50}$	99, 75[e]	75	27.7	30.4	1.18

[a] PEG = poly(ethyleneglycol) methyl ether methacrylate, Tn = Tn-antigen glycan monomer **2**, subscript = target degree of polymerization; [b] determined by ^{1}H NMR spectroscopy by comparison of the integrals of the monomer alkene peaks to a selected polymer peak in the spectrum of the crude polymer; [c] theoretical M_n, at observed conversion, determined from $[monomer]_0$:$[CTA]_0$; [d] determined by SEC; [e] values refer to copolymer first and second block respectively.

Glyconanoparticle Synthesis

Glyconanoparticles were synthesized using quantities of reagents detailed in Table S3. Separate solutions of $HAuCl_4$ (0.5 mM), glycopolymer (5.0 mM) and sodium borohydride (50 mM) were prepared in UHQ water (resistivity < 18.0 M). The $HAuCl_4$ and glycopolymer solutions were combined and then treated with $NaBH_4$ solution. An immediate solution colour change from yellow to pale brown was observed in

all cases. Stirring was continued for 2.5 h after which the nanoparticle solutions were purified by centrifugal filtration (Sartorious Vivaspin 15R, MWCO 30 kDa) and washing with UHQ water.

Table S3. Quantities of Reagents Used in the Preparation of Glyconanoparticles

Polymer[a]	Vol. $HAuCl_4$ (cm^3)[b]	Vol. Poly (cm^3)[c]	Polymer (g)	Vol. $NaBH_4$ (cm^3)[d]	Au:poly[e]
Tn_{50}	5	0.1	0.0071	1.0	2.5
$PEG_{40}Tn_{10}$	5	0.1	0.0075	1.0	2.5
$PEG_{25}Tn_{25}$	5	0.1	0.0085	1.0	2.5
$PEG_{80}Tn_{20}$	5	0.1	0.02	1.0	2.5
$PEG_{50}Tn_{50}$	2.5	0.05	0.0076	0.5	2.5

[a] PEG = poly(ethyleneglycol) methyl ether methacrylate, Tn = Tn-antigen glycan monomer **3**, subscript = target degree of polymerization; [b] $[HAuCl_4]$ = 0.5mM; [c] [Polymer] = 5.0mM; [d] $[NaBH_4]$ = 50mM; [e] Based on Au content of 49% for $HAuCl_4$.

Preparation of Asialo-Bovine Submaxillary Mucin

Bovine submaxillary mucin (BSM) was desialylated following the procedure described by O'Boyle et al.[3] Briefly, BSM was heated in 0.1N sulfuric acid solution for 1 h, dialysed against ultrapure water (3 x 2L) then freeze-dried and stored at -18 ^{o}C.

Nanoparticle Characterisation

TEM images of glyconanoparticle samples are shown in Figure S1.

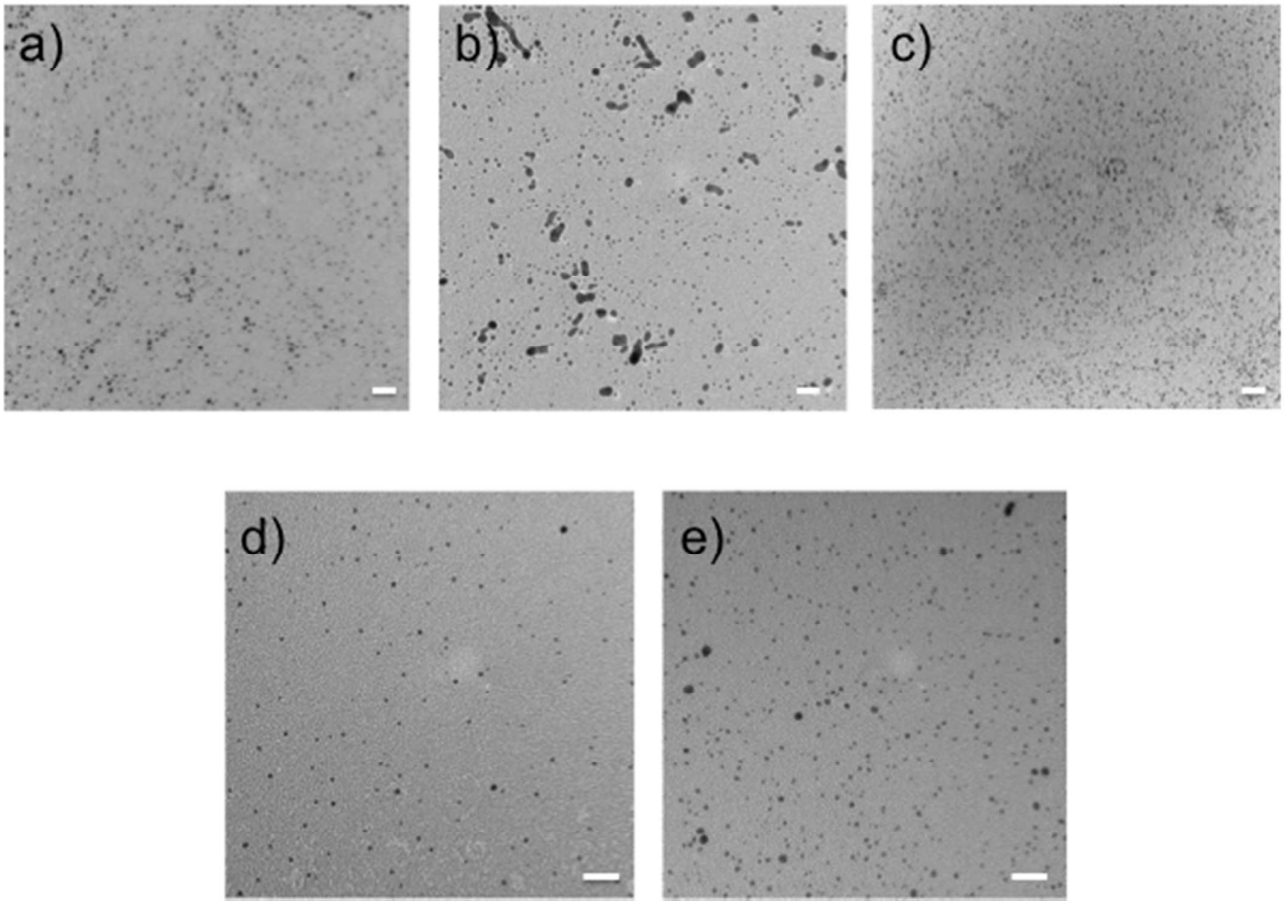


Figure S1. TEM images of glyconanoparticle samples prepared with different glycopolymer coronas: a) Tn_{50}; b) $PEG_{40}Tn_{10}$; c) $PEG_{25}Tn_{25}$; d) $PEG_{80}Tn_{20}$; e) $PEG_{50}Tn_{50}$. PEG = poly(ethyleneglycol) methyl ether methacrylate, Tn = Tn-antigen glycan monomer **2**, subscript = target degree of polymerization. Scale bar = 20 nm.

Dynamic light scattering traces are shown in Figure S2.

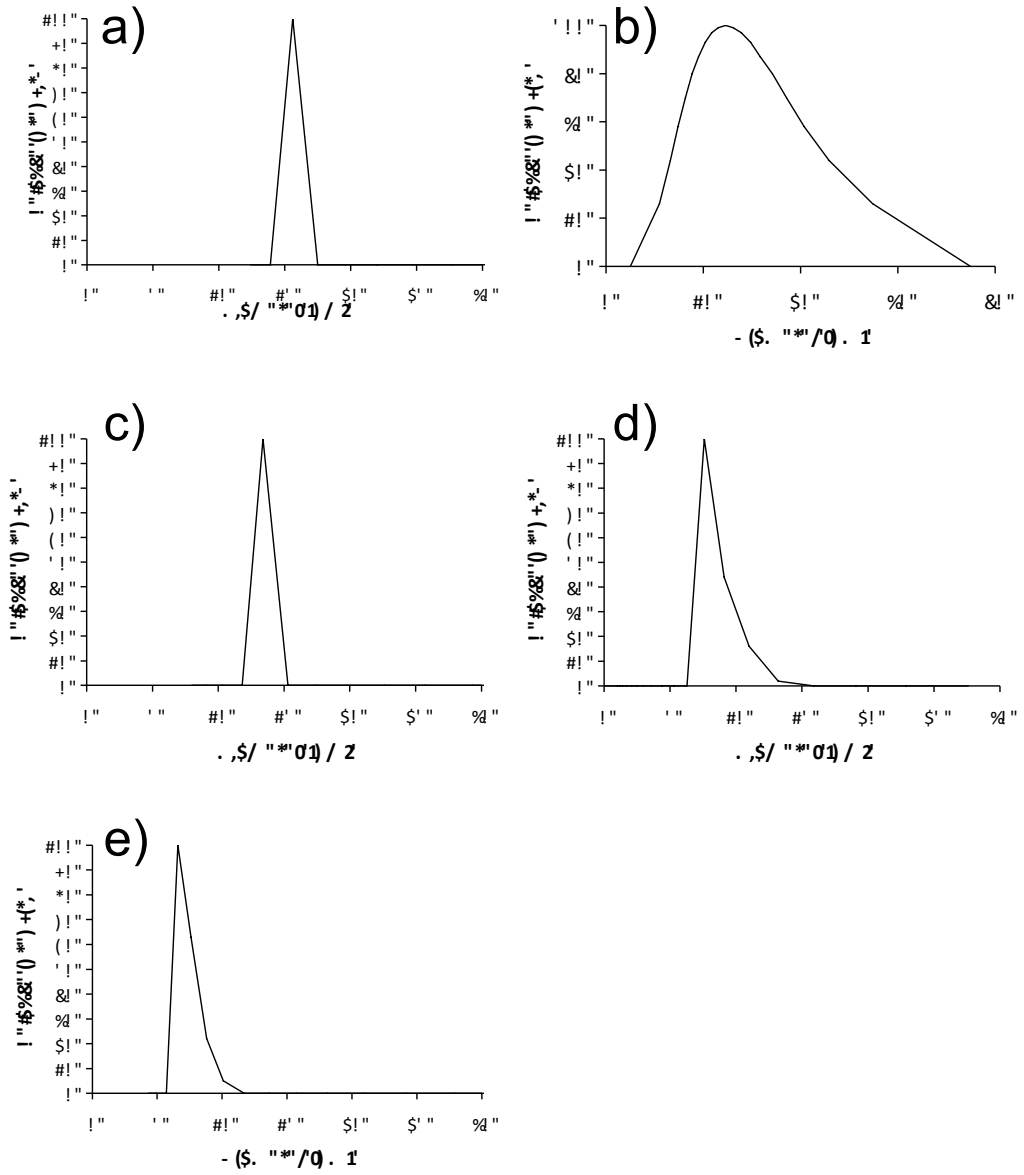


Figure S2. Dynamic light scattering traces for glyconanoparticle samples prepared with different glycopolymer coronas: a) Tn_{50}; b) $PEG_{40}Tn_{10}$; c) $PEG_{25}Tn_{25}$; d) $PEG_{80}Tn_{20}$; e) $PEG_{50}Tn_{50}$. PEG = poly(ethyleneglycol) methyl ether methacrylate, Tn = Tn-antigen glycan monomer **2**, subscript = target degree of polymerization.

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