Supporting Information

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SI Methods

General. All reagents were obtained from commercial sources and were used without purification unless otherwise stated. THF was distilled over Na/benzophenone or $NaHSO_3$/butylated hydroxytoluene immediately before use. Dry CH_2Cl_2 was obtained from a PureSolv-ENTM solvent purification system (Innovative Technology Inc.). All other anhydrous solvents were used as purchased from Sigma-Aldrich in AcroSeal bottles. Solvents and reagents were deoxygenated when necessary by purging with nitrogen. It is extremely important to note that NaN_3 is acute toxic and explosive. NaN_3 must be handled carefully, and contact with organic solvents and reagents containing leaving groups such as CH_2Cl_2 or $CHCl_3$ must be avoided. Milli-Q water obtained by Milli-Q UV plus with the resistivity 18.2 MΩ·cm was used for the preparation of PBS. PBS (1×) was obtained by dissolving 8 g of NaCl, 0.2 g of KCl, 1.44 g of Na_2HPO_4 and 0.24 g of KH_2PO_4 in 800 mL of Milli-Q water, adjusted to pH = 7.4 and diluted to 1,000 mL. The WT and engineered proteins were obtained by recombinant production and purification by affinity chromatography as a crucial step, in each case rigorously checked for purity by 1D and 2D gel electrophoresis, mass spectrometry including peptide fingerprinting, and gel filtration. Quaternary structure was also assessed by ultracentrifugation. Hemagglutination assays served as activity control. Respective protocols have been reported previously for WT Gal-1, Gal-3, Gal-4, and Gal-8 (S, L, F19Y variant) as well as CG-8S/L (1–4), the tetrameric form of human Gal-1 [$(Gal\text{-}1)_4$–GG)] (5), the Gal-4V/P variants with reduced linker length (6), and the Gal-3NT/8N variant (7).

Techniques. The ^1H and ^{13}C NMR spectra were recorded at 500 MHz/400 MHz and 126 MHz/101 MHz, respectively, on Bruker DRX 500 MHz or Varian-inova 500/400 MHz NMR spectrometer. All NMR spectra were measured at 25 °C in $CDCl_3$ or CD_3OD or D_2O. Chemical shifts (δ) are reported in parts per million, and coupling constants (*J*) are reported in hertz. The resonance multiplicities in the ^1H NMR spectra are described as "s" (singlet), "d" (doublet), "t" (triplet), "quint" (quintet), and "m" (multiplet), and broad resonances are indicated by "br." Residual protic solvent of $CDCl_3$ (^1H, δ 7.26 ppm; ^{13}C, δ 77.16 ppm), CD_3OD (^1H, δ 3.31 ppm; ^{13}C, δ 49.00 ppm), D_2O (^1H, δ 4.79 ppm), or tetramethylsilane (^1H, δ 0.00 ppm) was used as the internal reference in the ^1H- and ^{13}C-NMR spectra. The absorptions are given in wavenumbers (per centimeter). Assignments were aided by homonuclear ^1H-^1H (COSY, TOCSY), and ^1H-^{13}C heteronuclear (HSQC, HMBC) 2D correlation spectroscopies. Evolution of the reaction was monitored by TLC using silica gel 60 F_{254} precoated plates (E. Merck), and compounds were visualized by UV light with a wavelength of 254 nm, and/or by staining with an 8% H_2SO_4 dip (stock solution: 8 mL of conc. H_2SO_4, 92 mL of EtOH. Purifications by flash column chromatography were performed using flash silica gel from Silicycle or Davisil LC60A (60 Å, 40 μm to 63 μm), or with automated flash chromatography system, Buchi Reveleris X2 (UV 200 nm to 500 nm and evaporative light scattering detector (ELSD) detection, Reveleris silica cartiges 40 μm; BÜCHI Labortechnik AG) with the indicated eluent. The purity of the products was determined by a combination of TLC and HPLC using a Perkin-Elmer Series 10 high-pressure liquid chromatograph equipped with an LC-100 column oven, Nelson Analytical 900 Series integrator data station, and two Perkin-Elmer PL gel columns of 5×10^2 Å and 1×10^4 Å. Detection was done by refractive index or UV absorbance at 254 nm. Optical rotations were recorded on a Perkin-Elmer polarimeter (Model 343) at the sodium D-line (589 nm) at 20 °C using a 1-dm cell. Samples were prepared at the concentration (grams per milliliter) in the solvent indicated. High-resolution mass spectrometry data were recorded on a Waters micromass LCT LC-T of instrument using electrospray ionization in either positive or negative mode. MALDI-TOF mass spectrometry was performed on a PerSeptive Biosystem-Voyager-DE mass spectrometer equipped with a nitrogen laser (337 nm) and operating in linear mode. Internal calibration was performed using Angiotensin II and Bombesin as standards. The analytical sample was obtained by mixing the THF solution of the sample (5 mg/mL to 10 mg/mL) and THF solution of the matrix (2,5-dihydroxybenzoic acid, 10 mg/mL) in a 1/5 (vol/vol) ratio. The prepared solution of the sample and the matrix (2 μL) was loaded on the MALDI plate and allowed to dry at 23 °C before the plate was inserted into the vacuum chamber of the MALDI instrument. The laser steps and voltages applied were adjusted depending on both the molecular weight and the nature of each analyzed compound.

Synthesis. β-Lactose octaacetate (**1**) (8), 2-(3,4,5-Tris(((methyl triethylene glycol)benzoyl)oxy))-2,2-bis-hydroxymethyl-3-oxo-prop-2-yn-1-yl succinate (**7**) (9), JGD **3-Lac** (9), and **3-Man** (9) were prepared according to literature procedures.

The 2-(2-(2-Chloroethoxy)ethoxy)ethyl (2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside (2). β-Lactose octaacetate (**1**) (8) (15 g, 22.1 mmol) was dissolved in dry CH_2Cl_2 (184 mL) together with 2-(2-(2-chloroethoxy)ethoxy) ethanol (11 g, 66.3 mmol). The mixture was cooled to 0 °C, and $BF_3{\cdot}Et_2O$ (8 mL, 66.3 mmol) was slowly added over 15 min. The reaction was stirred overnight at 23 °C, then quenched with Et_3N until pH 7 and concentrated to dryness. Flash column chromatography (toluene/acetone, 9:1, vol/vol) gave compound **2** (14 g, 17.8 mmol, 80%) as a white foam. $R_f = 0.46$, toluene/acetone 7:3; $[\alpha]_D^{20} = -6.5$ (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.33 (dd, $J = 3.4$, 1.1 Hz, 1H, H-4′), 5.18 (*a*t, $J = 9.3$ Hz, 1H, H-3), 5.09 (dd, $J = 10.4$, 7.9 Hz, 1H, H-2′), 4.94 (dd, $J = 10.4$, 3.4 Hz, 1H, H-3′), 4.88 (dd, $J = 9.6$, 7.9 Hz, 1H, H-2), 4.56 (d, $J = 7.9$ Hz, 1H, H-1), 4.50 to 4.45 (m, 2H, H-1′, H-6a), 4.14 to 4.04 (m, 3H, H-6b, H-6′a, H-6′b), 3.93 to 3.82 (m, 2H, Glc-OC*H*H, H-5′), 3.78 (*a*t, $J =$ 9.5 Hz, 1H, H-4), 3.75 to 3.68 (m, 3H, Glc-OCH*H*, OCH_2CH_2Cl), 3.66 to 3.58 (m, 9H, OCH_2CH_2Cl, CH_2O, OCH_2CH_2O, H-5), 2.14 (s, 3H, $OCOCH_3$), 2.11 (s, 3H, $OCOCH_3$), 2.05 (s, 3H, $OCOCH_3$), 2.03 (s, 9H, 3 $OCOCH_3$), 1.95 (s, 3H, $OCOCH_3$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.5, 170.5, 170.3, 170.2, 169.9, 169.8, 169.2 (7 $OCOCH_3$), 101.2 (C-1′), 100.7 (C-1), 76.4 (C-4), 72.9 (C-3), 72.8 (C-5), 71.8 (C-2), 71.5 (OCH_2CH_2Cl), 71.1 (C-3′), 70.8 (C-5′), 70.8 (OCH_2CH_2O), 70.5 (CH_2O), 69.2 (C-2′), 69.2 (Glc-OCH_2), 66.7 (C-4′), 62.1 (C-6), 60.9 (C-6′), 42.90 (OCH_2CH_2Cl), 21.0, 20.9, 20.9, 20.8, 20.6 (7 $OCOCH_3$); HRMS (ESI^+): *m*/*z* calculated for $C_{32}H_{47}ClO_{20}$: 809.2247 $[M+Na]^+$; found 809.2242.

The 2-(2-(2-Azidoethoxy)ethoxy)ethyl (2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside (3). To a solution of compound **2** (14 g, 17.8 mmol) in DMF (200 mL) was added NaN_3 (6 g, 98 mmol). The reaction was stirred overnight at 80 °C, and then it was cooled to RT, evaporated, washed with H_2O, and extracted with EtOAc. Combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash column chromatography (toluene/acetone, 9:1, vol/vol) gave compound **3** (10.4 g, 13.1 mmol, 74%) as white foam. $R_f = 0.33$, toluene/acetone 8:2; $[\alpha]_D^{20} = -4.7$ (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.34 (dd, $J = 3.5$, 1.2 Hz, 1H, H-4′), 5.19 (*a*t, $J = 9.3$ Hz, 1H, H-3), 5.10 (dd, $J = 10.4$, 7.9 Hz, 1H, H-2′), 4.95 (dd, $J = 10.4$, 3.5 Hz, 1H, H-3′), 4.89 (dd, $J = 9.5$, 7.9 Hz, 1H,

H-2), 4.56 (d, J = 7.9 Hz, 1H, H-1), 4.51 to 4.45 (m, 2H, H-1′, H-6a), 4.15 to 4.04 (m, 3H, H-6b, H-6′a, H-6′b), 3.90 (ddd, J = 11.1, 4.9, 3.8 Hz, 1H, Glc-OCHH), 3.86 ($a$td, J = 6.9, 6.4, 1.2 Hz, 1H, H-5′), 3.78 (dd, J = 9.9, 9.0 Hz, 1H, H-4), 3.71 (ddd, J = 11.0, 6.9, 3.8 Hz, 1H, Glc-OCHH), 3.68 to 3.57 (m, 9H, OCH_2, OCH_2CH_2O, $OCH_2CH_2N_3$, H-5), 3.40 to 3.37 (m, 2H, $OCH_2CH_2N_3$), 2.14 (s, 3H, $OCOCH_3$), 2.11 (s, 3H, $OCOCH_3$), 2.05 (s, 3H, $OCOCH_3$), 2.04 to 2.03 (m, 9H, 3 $OCOCH_3$), 1.96 (s, 3H, $OCOCH_3$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.5, 170.5, 170.3, 170.2, 169.9, 169.8, 169.2 (7 $OCOCH_3$), 101.2 (C-1′), 100.8 (C-1), 76.4 (C-4), 72.9 (C-3), 72.8 (C-5), 71.8 (C-2), 71.1 (C-3′), 70.9, 70.8, 70.8, 70.5 (C-5′, $OCH_2CH_2N_3$, OCH_2CH_2O, OCH_2CH_2O), 70.2 (Glc-OCH_2CH_2), 69.3 (C-2′), 69.2 (Glc- OCH_2CH_2), 66.7 (C-4′), 62.2 (C-6), 60.9 (C-6′), 50.8 ($OCH_2CH_2N_3$), 21.0 ($OCOCH_3$), 20.9 ($OCOCH_3$), 20.8 ($OCOCH_3$), 20.8 ($OCOCH_3$), 20.8 ($OCOCH_3$), 20.7 ($OCOCH_3$), 20.7 ($OCOCH_3$); HRMS (ESI^+): m/z calculated for $C_{32}H_{47}N_3O_{20}$: 816.2651 $[M+Na]^+$; found 816.2636.

C2-(2-(2-Azidoethoxy)ethoxy)ethyl (β-D-galactopyranosyl)-(1 → 4)-β-D-glucopyranoside (4). Compound **3** (10.4 g, 13.1 mmol) was dissolved in MeOH (50 mL), and MeONa was added until pH 10. The reaction was stirred at 23 °C for 7 h, then neutralized with Dowex 50WX8 H^+ ion exchange resins until pH 7, filtered, and evaporated to give **4** (6.2 g, 12.4 mmol, 95%) as a white powder. R_f = 0.13, CH_2Cl_2/MeOH, 9:1; $[\alpha]_D^{20}$ = +0.7 (c 1.0, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 4.40 to 4.34 (m, 2H, H-1, H-1′), 4.03 (ddd, J = 10.7, 5.0, 3.4 Hz, 1H, Glc-OCHH), 3.93 (dd, J = 12.1, 2.5 Hz, 1H, H-6a), 3.89 to 3.77 (m, 4H, H-6b, H-6′a, Glc-OCHH, H-4′), 3.77 to 3.73 (m, 2H, H-6′b, OCH$H$$CH_2N_3$), 3.74 to 3.66 (m, 7H, OCHHCH_2N_3, CH_2O, OCH_2CH_2O), 3.64 to 3.53 (m, 4H, H-2′, H-5, H-4, H-3), 3.51 (dd, J = 9.7, 3.2 Hz, 1H, H-3′), 3.46 to 3.39 (m, 3H, H-5′, $OCH_2CH_2N_3$), 3.30 (at, J = 8.4 Hz, 1H, H-2); ^{13}C NMR (101 MHz, CD_3OD) δ 105.1 (C-1′), 104.3 (C-1), 80.6 (C-4), 77.1 (C-5), 76.5 (C-5′), 76.3 (C-3), 74.8 (C-2), 74.7 (C-3′), 72.5 (C-2′), 71.6, 71.5, 71.4, 71.1 ($OCH_2CH_2N_3$, OCH_2CH_2O, OCH_2CH_2O, Glc-OCH_2CH_2), 70.3 (C-4′), 69.7 (Glc-OCH_2CH_2), 62.5 (C-6′), 61.9 (C-6), 51.8 ($OCH_2CH_2N_3$); HRMS (ESI^+): m/z calculated for $C_{18}H_{33}N_3O_{13}$: 522.1911 $[M+Na]^+$; found 522.1924.

C2-(2-(2-Azidoethoxy)ethoxy)ethyl (2,4,6-tri-O-acetyl-3-O-sulfo-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside (5). Compound **4** (10) (1 g, 2 mmol) was dissolved in dry MeOH (16 mL) and reacted with Bu_2SnO (550 mg, 2.2 mmol) at 60 °C for 3 h. The reaction mixture was then cooled to 23 °C and concentrated in vacuo. The crude product was carefully dried in vacuum for 3 h, then dissolved in dry 1,4-dioxane (16 mL), $SO_3{\cdot}NMe_3$ complex (278 mg, 2 mmol) was added at 23 °C, and the mixture was stirred for 48 h. The reaction was then quenched with MeOH and concentrated to dryness. The crude sulfated product was acetylated overnight with Ac_2O (2.5 mL) in pyridine (5 mL). The mixture was then concentrated in vacuo, and the residue was purified by flash silica gel column chromatography (CH_2Cl_2/MeOH, 95:5, vol/vol) to afford the corresponding acetylated derivative **5** (1.1 g, 1.3 mmol, 65%) as white foam. R_f = 0.27, CH_2Cl_2/MeOH, 9:1; $[\alpha]_D^{20}$ = +6.2 (c 1.0, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 5.65 (ad, J = 3.5 Hz, 1H, H-4′), 5.22 (at, J = 9.3 Hz, 1H, H-3), 5.03 (dd, J = 10.1, 7.9 Hz, 1H, H-2′), 4.87 (under residual H_2O peak, H-2), 4.74 (d, J = 8.0 Hz, 1H, H-1), 4.72 (d, J = 8.0 Hz, 1H, H-1′), 4.62 to 4.54 (m, 2H, H-3′, H-6a), 4.23 to 4.04 (m, 4H, H-5′, H-6b, H-6′a, H-6′b), 3.97 to 3.86 (m, 2H, H-4, Glc-OCHH), 3.81 to 3.75 (m, 2H, Glc-OCHH, H-5), 3.74 to 3.66 (m, 8H, $OCH_2CH_2N_3$, OCH_2CH_2O, CH_2O), 3.45 to 3.40 (m, 2H, $OCH_2CH_2N_3$), 2.18 (s, 3H, $OCOCH_3$), 2.16 (s, 3H, $OCOCH_3$), 2.13 (s, 3H, $OCOCH_3$), 2.11 (s, 3H, $OCOCH_3$), 2.08 to 2.06 (m, 6H, 2 $OCOCH_3$); ^{13}C NMR (101 MHz, CD_3OD) δ 172.3, 172.2, 171.78, 171.7, 171.7, 171.4 (6 $OCOCH_3$), 102.2 (C-1′), 101.7 (C-1), 77.5 (C-4), 76.5 (C-3′), 74.5 (C-3), 74.0 (C-5), 73.2 (C-2), 72.3 (C-5′), 71.6, 71.5, 71.4 (C-2′, OCH_2CH_2O, Glc-OCH_2CH_2), 71.1 ($OCH_2CH_2N_3$), 70.1 (Glc-OCH_2CH_2O), 69.9 (C-4′), 63.5 (C-6), 63.0 (C-6′), 51.8 ($OCH_2CH_2N_3$), 21.1, 20.7, 20.7, 20.6 (6 $OCOCH_3$). HRMS (ESI^-): m/z calculated for $C_{30}H_{44}N_3O_{22}S$: 830.2137 $[M]^-$; found 830.2131.

The 2-(2-(2-Azidoethoxy)ethoxy)ethyl (3-O-sulfo-β-D-galactopyranosyl)-(1 → 4)-β-D-glucopyranoside (6). To a solution of **5** (4 g, 4.5 mmol) in MeOH (40 mL) was added MeONa until pH 12. The reaction mixture was stirred at 23 °C for 10 h, then neutralized with Dowex 50WX8 H^+ ion exchange resins, filtered, stirred with Dowex 50WX4 Na^+ form, filtered again, and concentrated to dryness to afford **6** (2.5 g, 4.1 mmol, 91%) as a white foam. R_f = 0.22, CH_2Cl_2/MeOH, 7:3; $[\alpha]_D^{20}$ = +50.5 (c 1.0, MeOH); ^{1}H NMR (500 MHz, D_2O) δ 4.59 (d, J = 7.9 Hz, 1H, H-1′), 4.55 (d, J = 8.0 Hz, 1H, H-1), 4.36 (dd, J = 9.9, 3.3 Hz, 1H, H-3′), 4.31 (ad, J = 3.3 Hz, 1H, H-4′), 4.09 (dt, J = 11.5, 4.2 Hz, 1H, Glc-OCHH), 4.01 (dd, J = 12.4, 2.2 Hz, 1H, H-6a), 3.90 to 3.66 (m, 16H, H-6b, H-6′a, H-6′b, Glc-OCHH, CH_2O, OCH_2CH_2O, $OCH_2CH_2N_3$, H-5′, H-2′, H-3, H-4), 3.62 (ddd, J = 9.6, 5.2, 2.2 Hz, 1H, H-5), 3.56 to 3.51 (m, 2H, $OCH_2CH_2N_3$), 3.37 (at, J = 8.4 Hz, 1H, H-2); ^{13}C NMR (126 MHz, D_2O) δ 102.5 (C-1′), 102.1 (C-1), 79.9 (C-3′), 78.3 (C-4), 74.9 (C-5′), 74.7 (C-5), 74.3 (C-3), 72.8 (C-2), 69.6, 69.5, 69.4, 69.2 (Glc-OCH_2CH_2O, OCH_2CH_2O, $OCH_2CH_2N_3$), 69.1 (C-2′), 68.7 (Glc-OCH_2CH_2O), 66.8 (C-4′), 60.9 (C-6′), 60.0 (C-6), 50.1 ($OCH_2CH_2N_3$); HRMS (ESI^-): m/z calculated for $C_{18}H_{32}N_3O_{16}S$: 578.1503 $[M]^-$; found 578.1479.

JGD 3-Sulfo-Lac. To a mixed solution of compound **7** (320 mg, 0.182 mmol) in THF (20 mL) and **6** (109 mg, 0.182 mmol) in water (2 mL) was added $CuSO_4{\cdot}5H_2O$ (46 mg, 0.182 mmol) in water (2 mL), and sodium ascorbate (72 mg, 0.364 mmol) in water (2 mL), successively, under nitrogen atmosphere. The reaction mixture was allowed to stir at 23 °C for 24 h. The reaction mixture was concentrated to dryness. The crude product was further purified by silica column chromatography with a mobile phase of CH_2Cl_2/MeOH, 10:1 to 4:1 to yield compound **3-Sulfo-Lac** as a colorless gel (240 mg, 55%). Purity (HPLC): 99%+. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.81 [s, 1H, 1×=CH (triazole)], 7.28 (s, 2H, 2×ArH), 7.06 (s, 4H, 4×ArH), 6.89 (br, 1H, 1×NH), 6.58 (s, 2H, 2×ArH), 5.14 (br, 2H, 1×O-CH_2-TRZ), 4.84 (m, 6H, 3×CH_2), 4.55 (m, 2H, 1×-OCH_2CH_2-N_{TRZ}), 4.36 (m, 2H), 4.18 to 4.23 (m, 6H), 3.52 to 3.89 (m, 60H) 3.37 (m, 9H, 3×OCH_3), 2.64 (br, 2H, 1×COO-CH_2CH_2CONH), 2.56 (m, 2H, COO-CH_2CH_2CONH), 1.72 to 1.75 [m, 8H, 4×-$ArCH_2CH_2CH_2(CH_2)_8CH_3$], 1.40 to 1.42 [m, 8H, 4×-$ArCH_2CH_2CH_2(CH_2)_8CH_3$], 1.25 to 1.29 [m, 64H, 4×-$ArCH_2CH_2CH_2(CH_2)_8CH_3$], 0.85 to 0.88 [t, J = 6.9 Hz, 12H, 4×-$Ar(CH_2)_{11}CH_3$]; ^{13}C NMR (126 MHz, $CDCl_3$) δ = 172.7, 172.4, 166.1, 165.8, 160.2, 152.3, 142.5, 131.1, 124.9, 124.4, 109.1, 107.8, 106.7, 103.2, 102.6, 79.9, 79.2, 74.8, 73.1, 72.4, 71.9, 70.7, 70.6, 70.4, 70.2, 69.6, 69.4, 68.4, 67.4, 64.0, 61.4, 60.9, 59.0, 59.0, 58.9, 57.9, 50.3, 32.0, 31.1, 29.7, 29.7, 29.7, 29.5, 29.4, 29.3, 26.1, 22.8, 14.2. MALDITOF (m/z): $[M+Na]^+$ calculated for $C_{119}H_{199}N_4Na_2O_{41}S$, 2,418.3; found 2,418.9.

NMR spectra of JGDs. Figs. S2 and S3 show the ^{1}H NMR spectrum of **3-Sulfo-Lac** ($CDCl_3$, 500 MHz) and ^{13}C NMR spectrum of **3-Sulfo-Lac** ($CDCl_3$, 126 MHz), respectively.

Cryo-TEM. Cryo-TEM was performed on a JEOL 2100 microscope at voltage of 200 kV. Briefly, a droplet of 2.5 μL of dendrimersome solution was pipetted onto a lacey carbon film coated on a copper TEM grid (300 mesh; Electron Microscopy Services) loaded into a Gatan Cp3 cryoplunger (Gatan). The sample was blotted by hand, then quickly plunged into liquefied ethane (~90 K) cooled by a reservoir of liquid nitrogen to ensure the vitrification of water. The vitrified samples were transferred to a Gatan CT3500TR single tilt cryo-transfer holder in a cryo-transfer stage immersed in liquid nitrogen. During the imaging, the cryo-holder was kept below –170 °C to prevent sublimation of vitreous solvent. The digital images were recorded with an Orius SC200 camera using SerialEM software. Image processing and analysis were completed with ImageJ 1.50 software.

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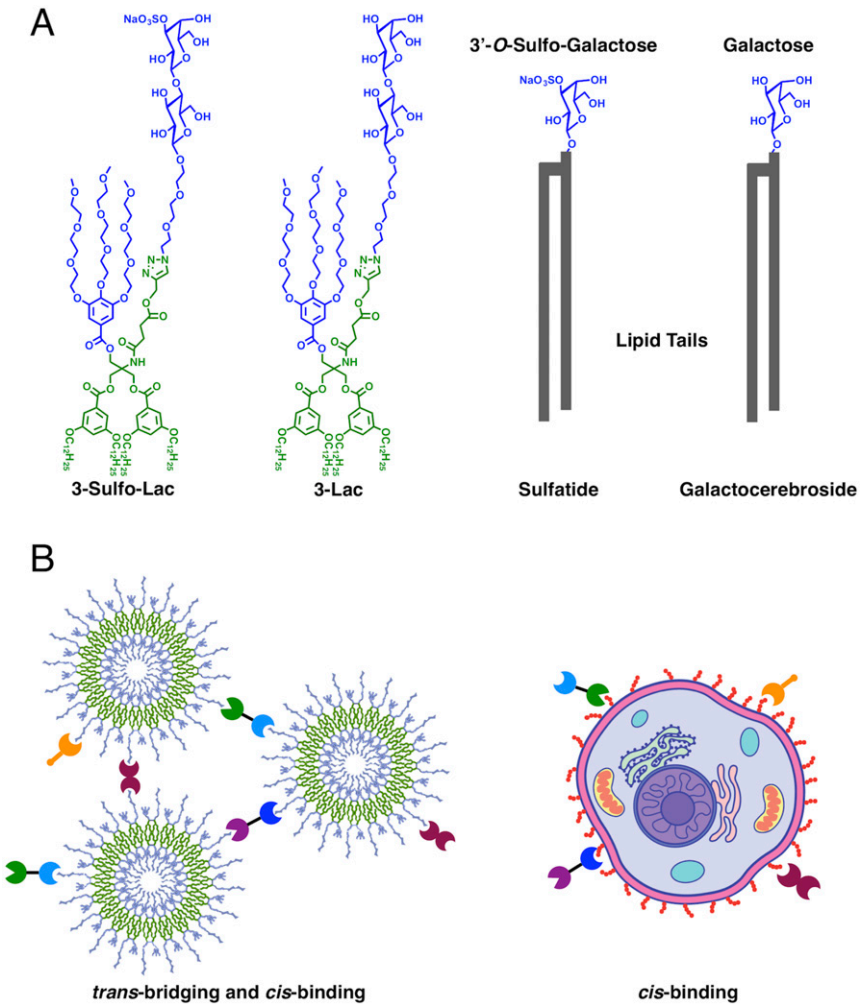


Fig. S1. Chemical structures of **3-Sulfo-Lac** and **3-Lac**, and illustrations of natural sulfatide and galactocerebroside (*A*). Illustration of *trans*-bridging and *cis*-binding of GDSs with galectins, and *cis*-binding of cells with galectins (*B*).

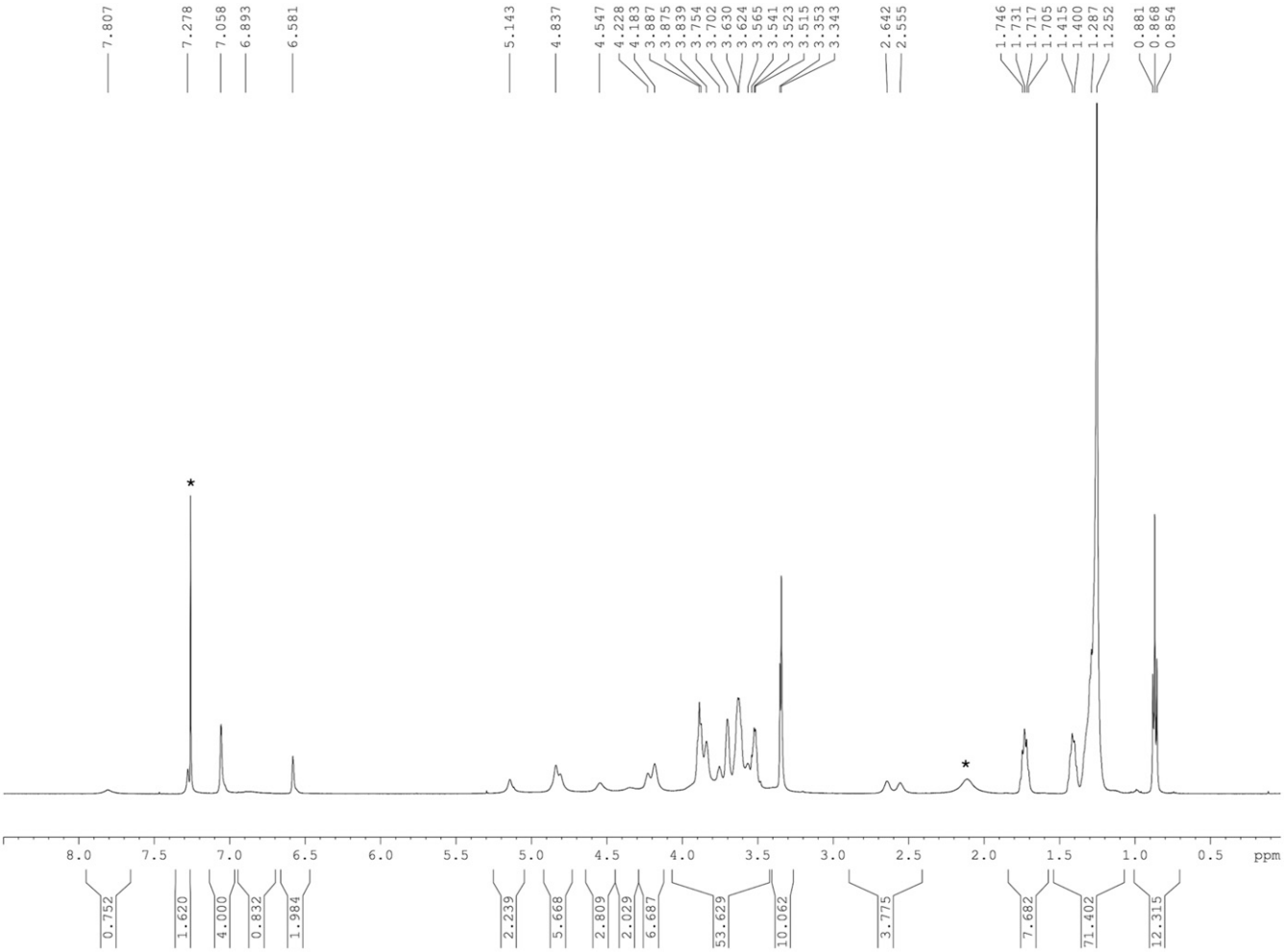


Fig. S2. The ^{1}H NMR spectrum of **3-Sulfo-Lac** ($CDCl_3$, 500 MHz). Asterisked signals at δ 7.26 ppm and 2.11 ppm are due to partially nondeuterated residues of $CDCl_3$ and water, respectively.

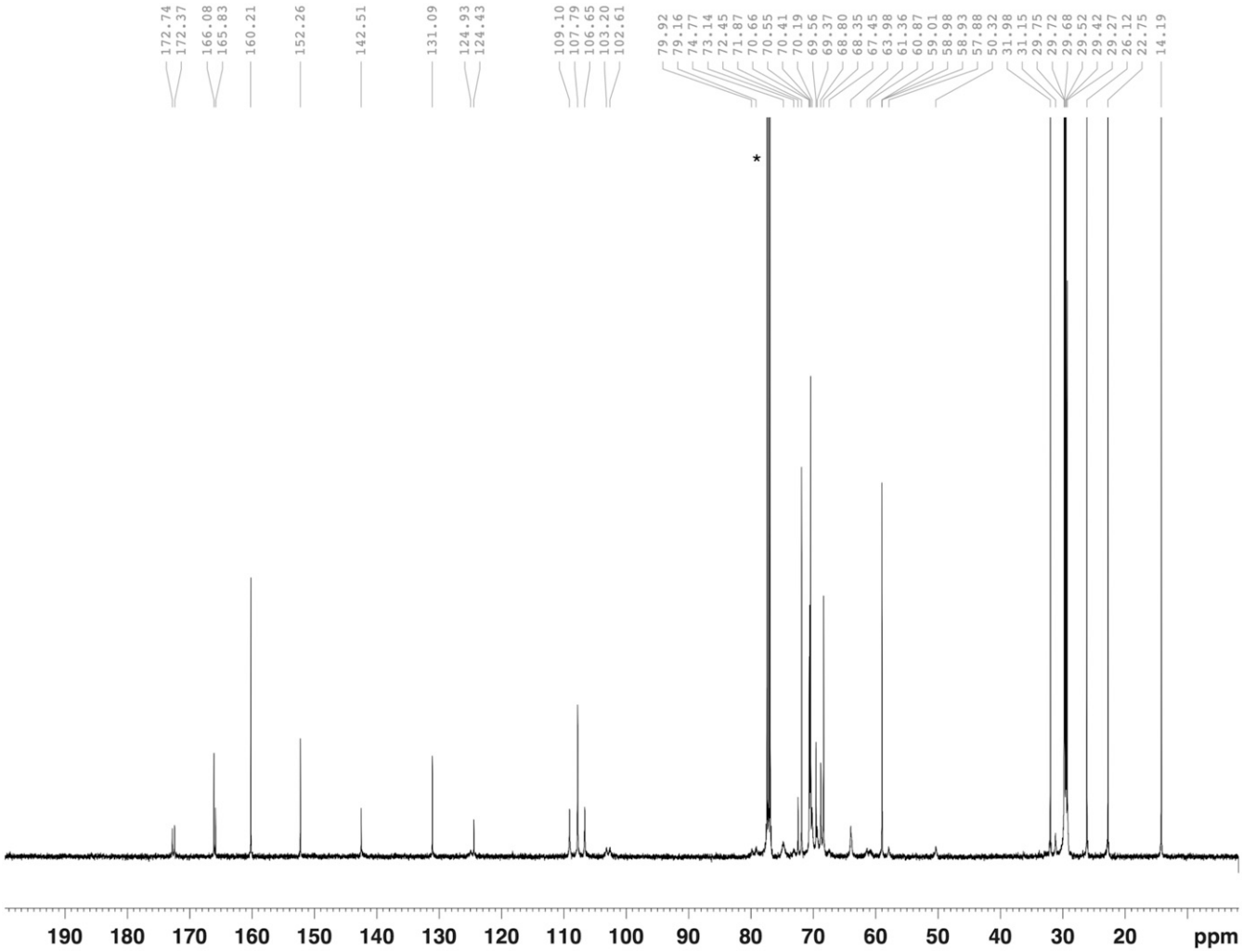


Fig. S3. The ^{13}C NMR spectrum of **3-Sulfo-Lac** ($CDCl_3$, 126 MHz). Asterisked signal at δ 77.16 ppm is due to $CDCl_3$.

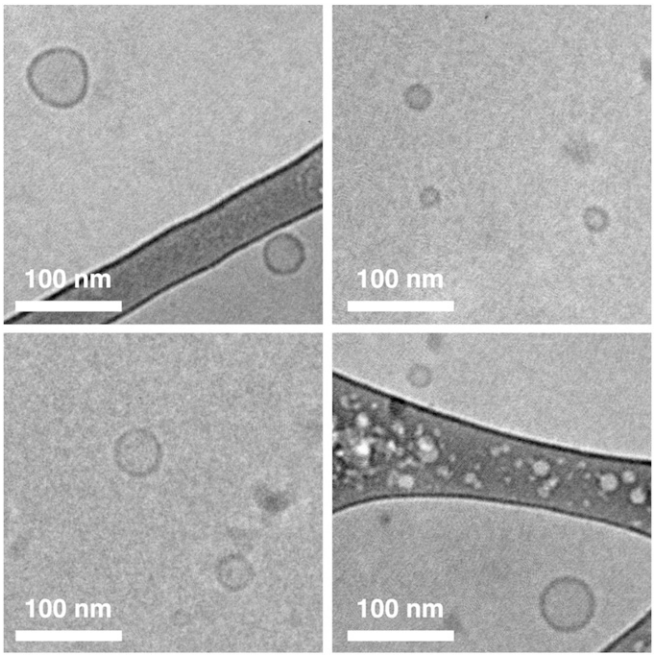


Fig. S4. Representative cryo-TEM images of GDS self-assembled from **3-Sulfo-Lac** (0.1 mM) by injection of THF solution into PBS (1×, pH 7.4).

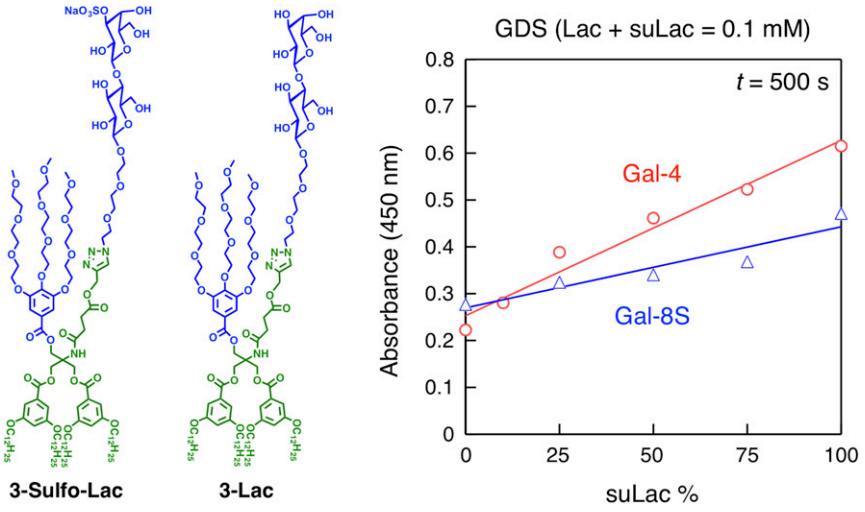


Fig. S5. Plots of the absorbance from aggregation of GDSs coassembled from **3-Sulfo-Lac** and **3-Lac** (suLac + Lac = 0.1 mM, 900 μL) with Gal-4 (red) and Gal-8S (blue) (2 mg·mL^{-1}, 100 μL) in PBS (pH 7.4) at t = 500 s, plotted from the data in Fig. 4 *C* and *D*.

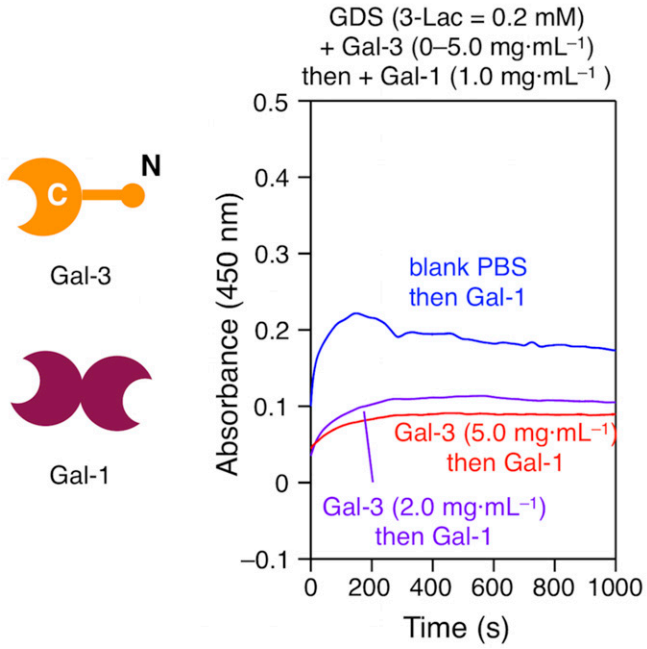
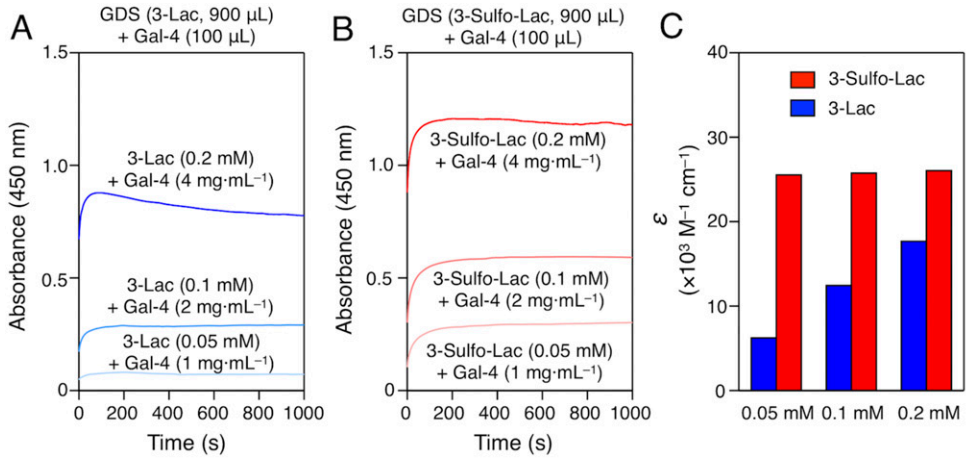


Fig. S6. Aggregation of GDSs (0.1 mM of **3-Lac**, 900 μL) with Gal-1 (2.0 mg·mL^{-1}, 100 μL) in PBS (pH 7.4); Gal-3 (0 mg·mL^{-1} to 5 mg·mL^{-1}, 100 μL) was added before the aggregation and incubated for 2 min.



D_{DLS} and PDI

	3-Lac	3-Sulfo-Lac
0.05 mM	44 nm (0.30)	33 nm (0.30)
0.1 mM	51 nm (0.24)	38 nm (0.23)
0.2 mM	71 nm (0.25)	47 nm (0.17)

Fig. S7. Aggregation of GDSs of **3-Lac** (*A*) or **3-Sulfo-Lac** (*B*) (0.05 mM to 0.2 mM, 900 μL) with Gal-4 (1.0 mg·mL^{-1} to 4.0 mg·mL^{-1}, 100 μL) in PBS (pH 7.4). Molar attenuation coefficient ε (*C*) is determined by the Beer–Lambert law, $\varepsilon = A \cdot (cl)^{-1}$, where *A*, is plateau value of absorbance, *c*, is molar concentration of Lac or suLac, and *l*, is semimicro cuvette path length (0.23 cm). The diameter (D_{DLS}) and PDI were determined by DLS.