Electronic Supplementary Information (ESI)

Gold nanoparticles decorated with monosaccharides and sulfated ligands as potential modulators of the lysosomal enzyme *N*-acetylgalactosamine-6-sulfatase (GALNS)

Francesca Buco,[a] Camilla Matassini,[a,*] Costanza Vanni,[a] Francesca Clemente,[a] Paolo Paoli,[b] Cosimo Carozzini,[a] Alice Beni,[a] Francesca Cardona,[a] Andrea Goti,[a] Sergio Enrique Moya,[c] Maria Grazia Ortore,[d] Patrizia Andreozzi,[a] Amelia Morrone[e] and Marco Marradi[a,*]

[a] *Department of Chemistry 'Ugo Schiff', University of Firenze, via della Lastruccia 13, Sesto Fiorentino, FI, Italy. E-mail: marco.marradi@unifi.it, camilla.matassini@unifi.it*
[b] *Department of Experimental and Clinical Biomedical Sciences, University of Florence, Viale Morgagni 50, 50134 Firenze, Italy*
[c] *CIC biomaGUNE, Basque Research and Technology Alliance (BRTA), Paseo Miramon 182 C, Donostia-San Sebastián 20014, Spain*
[d] *Department of Life and Environmental Sciences, Marche Polytechnic University, Via Brecce Bianche, Ancona, I-60130, Italy*
[e] *Paediatric Neurology Unit and Laboratories, Neuroscience Department, Meyer Children's Hospital, and Department of Neurosciences, Pharmacology and Child Health. University of Florence, Viale Pieraccini 24, 50139 Firenze, Italy*

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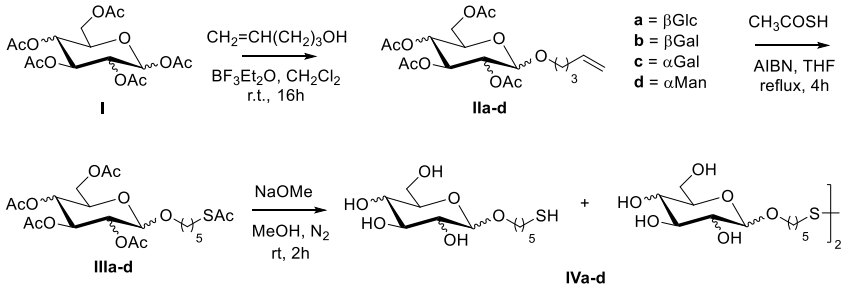
1. General

Commercial reagents were used as received. All reactions were carried out under magnetic stirring and monitored by TLC on 0.25 mm silica gel plates (Merck F254). Column chromatographies were carried out on Silica Gel 60 (32–63 μm) or on silica gel (230–400 mesh, Merck). Yields refer to spectroscopically and analytically pure compounds unless otherwise stated. ^{1}H NMR spectra were recorded on a Varian Mercury-400 or on a Varian INOVA-400 instruments at 25 °C. ^{13}C NMR spectra were recorded on a Varian Mercury-400 or on a Varian Gemini-200. Chemical shifts are reported relative to $CDCl_3$ (^{13}C: δ = 77.0 ppm, ^{1}H: 7.26 ppm), CD_3OD (^{13}C: δ = 49.0 ppm, ^{1}H: δ = 3.31 ppm), or D_2O (^{1}H: δ = 4.79 ppm). Integrals are in accordance with assignments, coupling constants are given in Hz. Splitting patterns are described by using the following abbreviations: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. For detailed peak assignments 2D spectra were measured (gCOSY, gHSQC). UV-Vis spectra were measured with a Varian CaryWin 4000 UV/Vis spectrophotometer. TEM analysis was performed with a JEOL JEM-2100Fmicroscope, operating at 200 kV. IR spectra were recorded with a IRAffinity-1S Shimadzu spectrophotometer or with a FTIR-8400S Shimadzu spectrophotometer. ESI MS spectra were recorded with a Thermo Scientific™ LCQ fleet ion trap mass spectrometer. Elemental analyses were performed with a Thermoscientific FlashSmart Elemental Analyzer CHNS/O. Optical rotation measurements were performed on a JASCO DIP-370 polarimeter.

Acronyms anad main abbreviations:
AcOEt= ethyl acetate, AIBN= 2,2'-azobis(2-methyl-propionitrile), CH_3COSH= thioacetic acid, EtP= petroleum ether, FCC= flash column chromatography, R_f= retention factor, r.t.= room temperature, SPR= surface plasmon resonance, THF= tetrahydrofuran, TLC= thin layer chromatography.

1.1 Synthesis of thiol-ending glycoside ligands



Scheme S1*. General scheme for the preparation of the thiol-ending glycosides, which were obtained as a mixture of thiol and disulfide, starting from commercially available peracetylated sugars.*

1.1.1 General procedure for the synthesis of pent-4-enyl 2,3,4,6-tetra-O-acetyl-glycosides (II)

To a solution of peracetylated sugar **I** (1 eq.) and 4-penten-1-ol (4 eq.) in dry CH_2Cl_2 (0.3M), $BF_3{\cdot}Et_2O$ (7 eq.) was added at 0°C. The reaction mixture was allowed to return at room temperature and stirred under inert atmosphere for 16 h. After the disappearance of the starting material and the appearance of a new product attested by TLC, a solution of $NaHCO_3$ was added until pH=7. The organic layer was then washed with $NaHCO_3$ (3x20 mL), H_2O (1x30 mL) and brine (1x30 mL). The reaction crude was purified through FCC to obtain the pure product **II**.

Pent-4-enyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (IIa) [1,2]**:** Starting from β-D-glucose pentaacetate **I** (1.00 g, 2.56 mmol), 4-penten-1-ol (1.05 mL, 10.2 mmol) and $BF_3{\cdot}Et_2O$ (2.27 mL, 17.92 mmol), compound **IIa** was obtained as a colorless oil (0.506 g, 1.22 mmol, 47%). **R_f** (EtP/AcOEt = 1.75/1) = 0.48. **^{1}H NMR ($CDCl_3$, 200 MHz):** δ 5.78 (ddt, *J* = 17.0, 10.1, 6.7 Hz, 1H, $OCH_2CH_2CH_2CH = CH_2$), 5.36-4.87 (m, 5H, H-2, H-3, H-4, and $OCH_2CH_2CH_2CH = CH_2$), 4.49 (d, *J* = 7.9 Hz, 1H, *anomeric*), 4.36-4.03 (m, 2H, H-6), 3.97-3.82 (m, 1H, $OCH_aCH_2CH_2CH_2 = CH_2$), 3.69 (ddd, *J* = 9.5, 4.5, 2.4 Hz, 1H, H-5), 3.58-3.39 (m, 1H, $OCH_bCH_2CH_2CH_2 = CH_2$), 2.09 (s, 3H, CH_3C=O), 2.05 (s, 3H, CH_3C=O), 2.03 (s, 3H, CH_3C=O), 201 (s, 3H,

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C*H*$_3$C=O), 1.80-1.59 (m, 2H, OCH$_2$CH$_2$C*H*$_2$CH=CH$_2$) and 1.43-1.24 (m, 2H, OCH$_2$C*H*$_2$CH$_2$CH=CH$_2$). **MS** (ESI) m/z (%) = calc. for $C_{19}H_{28}O_{10}Na^+$ [*M*+Na]$^+$: 439.16; found: 439.29 (100%).

Pent-4-enyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (IIb)[2,3] **and Pent-4-enyl 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranoside (IIc)**[2]**:** Starting from β-D-galactose pentaacetate **I** (4.00 g, 10.25 mmol), 4-penten-1-ol (4.15 mL, 40.99 mmol) and $BF_3{\cdot}Et_2O$ (8.85 mL, 71.73 mmol), the β anomer **IIb** (1.64 g, 3.94 mmol, 38%) and the α anomer **IIc** (0.85 g, 2.04 mmol, 20%) were obtained as colorless oils.

IIb: R$_f$ (EtP/AcOEt = 2/1) = 0.60. **^{1}H NMR (CDCl$_3$, 400 MHz):** δ 5.78 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H, OCH$_2$CH$_2$CH$_2$C*H*=CH$_2$), 5.38 (dd, *J* = 3.5, 1.1 Hz, 1H, H-4), 5.20 (dd, *J* = 10.5, 7.9 Hz, 1H, H-2), 5.06-4.94 (m, 3H, H-3 and OCH$_2$CH$_2$CH$_2$CH = C*H*$_2$), 4.45 (d, *J* = 7.9 Hz, 1H, *anomeric*), 4.26-4.05 (m, 2H, H-6), 4.26-4.05 (m, 2H, H-5 and OC*H*$_a$CH$_2$CH$_2$CH = CH$_2$), 3.49 (ddd, *J* = 9.7, 7.4, 6.2 Hz, 1H, OC*H*$_b$CH$_2$CH$_2$CH = CH$_2$), 2.17-2.01 (m, 2H, OCH$_2$CH$_2$C*H*$_2$CH = CH$_2$), 2.14 (s, 3H, C*H*$_3$C=O), 2.05 (s, 3H, C*H*$_3$C=O), 2.04 (s, 3H, C*H*$_3$C=O), 1.98 (s, 3H, C*H*$_3$C=O), 1.77-1.61 (m, 2H, OCH$_2$C*H*$_2$CH$_2$CH = CH$_2$). **MS** (ESI) m/z (%) = *m/z*: calc. for $C_{19}H_{28}O_{10}H^+$ [*M*+H]$^+$: 413.16; found: 413.30 (100%). **IR** $\tilde{\nu}$ 1743, 1215 cm^{-1}.

IIc: R$_f$ (EtP/AcOEt = 2/1) = 0.63. **^{1}H NMR (CDCl$_3$, 400 MHz):** δ 5.80 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H, OCH$_2$CH$_2$CH$_2$C*H* = CH$_2$), 5.45 (dd, *J* = 3.4, 1.3 Hz, 1H, H-4), 5.38-5.29 (m, 1H, H-3), 5.13-5.11 (m, 1H, H-2), 5.09 (d, *J* = 2.6 Hz, 1H, *anomeric*), 5.06-4.95 (m, 2H, OCH$_2$CH$_2$CH$_2$CH = C*H*$_2$), 4.21 (td, *J* = 6.5, 6.1, 1.3 Hz, 1H, H-5), 4.09 (dd, *J* = 6.6, 1.9 Hz, 2H, H-6), 3.69 (dt, *J* = 9.8, 6.4 Hz, 1H, OC*H*$_a$CH$_2$CH$_2$CH$_2$ = CH$_2$), 3.43 (dt, *J* = 9.8, 6.5 Hz, 1H, OC*H*$_b$CH$_2$CH$_2$CH = CH$_2$), 2.16-2.07 (m, 2H, OCH$_2$CH$_2$C*H*$_2$CH = CH$_2$), 2.13 (s, 3H, C*H*$_3$C=O), 2.07 (s, 3H, C*H*$_3$C=O), 2.04 (s, 3H, C*H*$_3$C=O), 1.98 (s, 3H, C*H*$_3$C=O), 1.69 (p, *J* = 6.8 Hz, 2H, OCH$_2$C*H*$_2$CH$_2$CH = CH$_2$). **MS** (ESI) m/z (%) = *m/z*: calc. for $C_{19}H_{28}O_{10}H^+$ [*M*+H]$^+$: 413.16; found: 413.27 (100%). **IR** $\tilde{\nu}$ 1743, 1215 cm^{-1}.

Pent-4-enyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (IId)[4]**:** Starting from α-D-mannose pentaacetate **I** (2.0 g, 5.12 mmol), 4-penten-1-ol (2.1 mL, 20.50 mmol) and $BF_3{\cdot}Et_2O$ (4.43 mL, 35.87 mmol), compound **IId** was obtained as a yellowish oil (0.93 g, 2.23 mmol, 43%). **R$_f$** (EtP/AcOEt = 2/1) = 0.5. **^{1}H NMR (CDCl$_3$, 200 MHz):** δ 5.91-5.70 (m, 1H, OCH$_2$CH$_2$CH$_2$C*H*=CH$_2$), 5.39-5.21 (m, 3H, *H*-2, *H*-3, *H*-4), 5.09-4.96 (m, 2H, OCH$_2$CH$_2$CH$_2$CH = C*H*$_2$), 4.80 (d, *J* = 2.0 Hz, 1H, *anomeric*), 4.32-3.95 (m, 3H, H-5, H-6), 3.76-3.64 (m, 1H, OC*H*$_a$CH$_2$CH$_2$CH=CH$_2$), 3.52-3.41 (m, 1H, OC*H*$_b$CH$_2$CH$_2$CH=CH$_2$), 2.18-1.97 (m, 14H, C*H*$_3$C=O, OCH$_2$CH$_2$C*H*$_2$CH=CH$_2$), 1.78-1.65 (m, 2H, OCH$_2$C*H*$_2$CH$_2$CH=CH$_2$).

1.1.2 General procedure for the synthesis of 5-(acetylthio) pentyl 2,3,4,6-tetra-O-acetyl-glycosides (III)

To a solution of pent-4-enyl 2,3,4,6-tetra-*O*-acetyl-glycoside **II** (1 eq.) in THF inhibitor free (0.1M), CH_3COSH (4 eq.) and AIBN (0.1 eq.) were added. The reaction mixture was heated to reflux for 2 h. After the disappearance of the starting material and the appearance of a new product attested by TLC, the solution was diluted with AcOEt and a solution of $NaHCO_3$ was added until pH=7. The organic layer was then washed with $NaHCO_3$ (2x20 mL) and brine (1x30 mL) and dried with Na_2SO_4. The residue was then purified through FCC to afford the pure product **III**.

5-(acetylthio)pentyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (IIIa)[5]**:** Starting from pent-4-enyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**IIa**) (286 mg, 0.69 mmol), CH_3COSH (0.20 mL, 2.76 mmol) and AIBN (11 mg, 0.07 mmol), pure **IIIa** was obtained after FCC (EtP/AcOEt 2.5:1) as yellow oil with 47% yield (160 mg, 0.324 mmol). **R$_f$** (EtP/AcOEt = 2/1) = 0.32. **^{1}H NMR (CDCl$_3$, 400 MHz)** δ 5.19 (t, *J* = 9.5 Hz, 1H, H-3), 5.08 (t, *J* = 9.7 Hz, 1H, H-4), 4.97 (dd, *J* = 9.6, 8.0 Hz, 1H, H-2), 4.48 (d, *J* = 8.0 Hz, 1H, *anomeric*), 4.30-4.21 (m, 1H, H-6a), 4.17-4.08 (m, 1H, H-6b), 3.86 (dt, *J* = 9.6, 6.2 Hz, 1H, OC*H*$_a$CH$_2$), 3.68 (ddd, *J* = 9.9, 4.7, 2.4 Hz, 1H, H-5), 3.47 (dt, *J* = 9.6, 6.6 Hz, 1H, OC*H*$_b$CH$_2$), 2.85 (t, *J* = 7.2 Hz, 2H, C*H*$_2$SAc), 2.32 (s, 3H, S(C=O)C*H*$_3$), 2.08 (s, 3H, C*H*$_3$C=O), 2.05 (s, 3H, C*H*$_3$C=O), 2.02 (s, 3H, C*H*$_3$C=O), 2.00 (s, 3H, C*H*$_3$C=O), 1.61-1.52 (m, 4H, OCH$_2$C*H*$_2$CH$_2$C*H*$_2$CH$_2$SAc) and 1.45-1.33 (m, 2H, OCH$_2$CH$_2$C*H*$_2$CH$_2$CH$_2$SAc). **MS** (ESI) m/z (%) = calc. per $C_{21}H_{32}O_{11}SNa^+$ [*M*+Na]$^+$: 515.16; found: 515.30 (100%).

5-(acetylthio)pentyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (IIIb)[6,7]**:** Starting from pent-4-enyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (**IIb**) (1.0 g, 2.40 mmol), CH_3COSH (687 μL, 9.61 mmol) and AIBN (39 mg, 0.24 mmol), pure **IIId** was obtained after FCC (EtP/AcOEt 1.5:1) as yellow oil with 93% yield (1.10 g, 2.24 mmol). **R$_f$** (EtP/AcOEt = 2/1) = 0.40. **^{1}H NMR (CDCl$_3$, 400 MHz):** δ 5.38 (dd, *J* = 3.4, 1.1 Hz, 1H, H-4), 5.20 (dd, *J* = 10.5, 7.8 Hz, 1H, H-2), 5.00 (dd, *J* = 10.5, 3.3 Hz, 1H, H-3), 4.44 (d, *J* = 7.9 Hz, 1H, *anomeric*), 4.25-4.04 (m, 2H, H-6), 3.96-3.78 (m, 2H, OC*H*$_a$CH$_2$ and H-5), 3.59-3.56 (m, 1H, OC*H*$_b$CH$_2$), 2.85 (t, *J* = 7.1 Hz, 2H, C*H*$_2$SAc), 2.32 (s, 3H, S(C=O)C*H*$_3$), 2.15 (s, 3H, C*H*$_3$C=O), 2.06 (s, 3H, C*H*$_3$C=O),

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2.05 (s, 3H, C*H*$_3$C=O), 198 (s, 3H, C*H*$_3$C=O), 1.68-1.31 (m, 6H, OCH$_2$C*H*$_2$C*H*$_2$C*H*$_2$CH$_2$SAc). **^{13}C NMR (CDCl$_3$, 100 MHz)** δ 195.8 (s, 1C, S(*C*=O)CH$_3$), 170.4 (s, 1C, CH$_3$*C*=O), 170.3 (s, 1C, CH$_3$*C*=O), 170.2 (s, 1C, CH$_3$*C*=O), 169.4 (s, 1C, CH$_3$*C*=O), 101.5 (d , 1C, *anomeric*), 71.2 and 70.8 (d, 2C, C-3 and C-5), 69.9 (t, 1C, O*C*H$_2$CH$_2$), 69.1 (d, 1C, C-2), 67.3 (d, 1C, C-4), 61.5 (t, 1C, C-6), 30.7 (q, 1C, S(C=O)*C*H$_3$), 29.3, 29.0, 29.0 and 28.9 (t, 4C, OCH$_2$*C*H$_2$*C*H$_2$*C*H$_2$*C*H$_2$SAc), 20.8 (q, 1C, *C*H$_3$C=O), 20.7 (q, 1C, *C*H$_3$C=O), 20.7 (q, 1C, *C*H$_3$C=O), 20.7 (q, 1C, *C*H$_3$C=O). **MS** (ESI) m/z (%) = *m/z*: calc. per $C_{21}H_{32}O_{11}SNa^+$ [*M*+Na]$^+$: 515.16; found: 515.24 (100%). **IR** $\tilde{\nu}$ 1745, 1688, 1215 cm^{-1}.

5-(acetylthio)pentyl 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranoside (IIIc): Starting from pent-4-enyl 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranoside (**IIc**) (143 mg, 0.343 mmol), CH$_3$COSH (104 mg, 1.37 mmol, 4 eq.) and AIBN (6.0 mg, 0.03 mmol), pure **IIIc** was obtained after FCC (gradient Hexane/AcOEt 2:1 to 3:2) as yellow oil with 59% yield (100 mg, 0.203 mmol). **R$_f$** = 0.45 (EtP/AcOEt 2:1). **[α]$_D^{22}$** +82° (MeOH, c = 0.54 g/100mL). **^{1}H NMR (CDCl$_3$, 400 MHz):** δ 5.44 (dd, *J* = 3.3, 1.6 Hz, 1H, H-4), 5.36–5.31 (m, 1H, H-3), 5.12–5.08 (m, 2H, H-2 and *anomeric*), 4.22-4.18 (m, 1H, H-5), 4.09 (d, *J*=6.53 Hz, H-6), 3.68 (dt, *J* = 9.8, 6.4 Hz, 1H, OC*H$_a$*CH$_2$), 3.41 (dt, *J* = 9.8, 6.5 Hz, 1H, OC*H$_b$*CH$_2$), 2.87 (t, *J* = 7.3 Hz, 2H, C*H$_2$*SAc), 2.32 (s, 3H, S(C=O)C*H$_3$*), 2.14 (s, 3H, C*H$_3$*C=O), 2.08 (s, 3H, C*H$_3$*C=O), 2.05 (s, 3H, C*H$_3$*C=O), 1.98 (s, 3H, C*H$_3$*C=O), 1.64–1.56 (m, 4H, OCH$_2$C*H$_2$*C*H$_2$*CH$_2$CH$_2$SAc), 1.46–1.40 (m, 2H, OCH$_2$CH$_2$CH$_2$C*H$_2$*CH$_2$SAc). **^{13}C NMR (CDCl$_3$, 100 MHz)** δ 196.0 (s, 1C, S(*C*=O)CH$_3$), 170.6 (s, 2C, 2 x CH$_3$*C*=O), 170.4 (s, 1C, CH$_3$*C*=O), 170.2 (s, 1C, CH$_3$*C*=O), 96.3 (d, 1C, *anomeric*), 68.4-68.3 (d, 2C, C-2 and C-4; t, 1C, O*C*H$_2$CH$_2$CH$_2$CH$_2$CH$_2$SAc), 67.8 (d, 1C, C-3), 66.3 (d, 1C, C-5), 62.0 (t, 1C, C-6), 30.8 (q, 1C, S(C=O)*C*H$_3$), 29.4, 29.1, 28.9 and 25.4 (t, 4C, OCH$_2$*C*H$_2$*C*H$_2$*C*H$_2$*C*H$_2$SAc), 20.9 (q, 1C, *C*H$_3$C=O), 20.9 (q, 1C, *C*H$_3$C=O), 20.8 (q, 1C, *C*H$_3$C=O), 20.8 (q, 1C, *C*H$_3$C=O). **MS** (ESI) m/z (%) = calc. for $C_{21}H_{32}O_{11}SNa^+$ [*M*+Na]$^+$: 515.16; found 515.32 (100%). **IR** $\tilde{\nu}$ 1744, 1688, 1217 cm^{-1}. **Elemental analysis**: Calc. (%) $C_{21}H_{32}O_{11}S$: C 51.21, H 6.55, S 6.51; Found: C 51.19, H 6.55, S 6.53.

5-(acetylthio)pentyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (IIId)[8]: Starting from pent-4-enyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (**IId**) (54.0 mg, 0.130 mmol), CH$_3$COSH (37 μL, 0.52 mmol) and AIBN (2.1 mg, 0.013 mmol), pure **IIId** was obtained after FCC (EtP/AcOEt 2:1) as yellow oil with 88% yield (56.0 mg, 0.114 mmol). **R$_f$** (EtP/AcOEt = 1.5/1) = 0.47. **^{1}H NMR (CDCl$_3$, 200 MHz)** δ 5.32-5.22 (m, 3H, H-2, H-3, H-4), 4.79 (d, *J* = 2 Hz, 1H, *anomeric*), 4.30-4.29 (m, 1H, H-5), 4.14-4.07 (m, 2H, H-6), 3.70-3.64 (m, 1H, OC*H*$_a$CH$_2$), 3.49-3.41 (m, 1H, OC*H*$_b$CH$_2$), 2.87 (t, *J* = 8 Hz, 2H, C*H$_2$*SAc), 2.32 (s, 3H, S(C=O)C*H$_3$*), 2.15-1.99 (m, 12H, C*H$_3$*C=O), 1.63-1.56 (m, 6H, OCH$_2$C*H$_2$*C*H$_2$*C*H$_2$*CH$_2$SAc).

1.1.3 General procedure for the synthesis of 5-(mercapto)pentyl glycosides (IV)

Sodium methanoate (1 eq.) was added to a solution of 5-(acetylthio) pentyl 2,3,4,6-tetra-*O*-acetyl-glycoside **III** in MeOH (0.02M). The reaction mixture was stirred under inert atmosphere at room temperature for 3h and then the strong acid resin Amberlist®15 ion-exchange was added until pH=7. The solution was filtered, the solvent removed under reduced pressure and the product was obtained as a mixture of thiol and its oxidized disulfide form **IV** and was used without further purification.

5-(mercapto)pentyl-β-D-glucopyranoside (IVa)[9]: Starting from 5-(acetylthio)pentyl 2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside (**IIIa**) (107 mg, 0.217 mmol) and NaOMe (11.7 mg, 0.217 mmol), **IVa** was obtained as yellow oil with 65% yield (40 mg, 0.142 mmol). **^{1}H NMR (CD$_3$OD, 200 MHz)** δ 4.25 (d, *J* = 7.7 Hz, 1H), 4.01-3.80 (m, 2H), 3.75-3.60 (m, 1H), 3.58-3.45 (m, 1H), 3.40-3.33 (m, 1H), 3.32-3.26 (m, 2H), 3.20-3.07 (m, 1H), 2.70 (t, *J* = 7.1 Hz, 1H, C*H$_2$*SS), 2.48 (t, *J* = 7.2 Hz, 1H, C*H$_2$*SH), 1.81-1.37 (m, 6H).

5-(mercapto)pentyl-β-D-galactopyranoside (IVb)[7]: Starting from 5-(acetylthio)pentyl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranoside (**IIIb**) (144 mg, 0.292 mmol) and NaOMe (15.8 mg, 0.292 mmol), **IVb** was obtained as yellow oil with 74% yield (60 mg, 0.216 mmol). **^{1}H NMR (CD$_3$OD, 200 MHz)** δ 4.21 (d, *J* = 6.5Hz, 1H, *anomeric*), 4.01-3.25 (m, 8H), 2.70 (t, *J* = 7.1 Hz, 0.8H, C*H$_2$*SS), 2.50 (t, *J* = 6.7 Hz, 1.2H, C*H$_2$*SH), 1.85-1.33 (m, 6H, OCH$_2$(C*H$_2$*)$_3$CH$_2$S).

5-(mercapto)pentyl-α-D-galactopyranoside (IVc): Starting from 5-(acetylthio)pentyl 2,3,4,6-tetra-O-acetyl-α-D-galactopyranoside (**IIIc**) (49 mg, 0.10 mmol) and NaOMe (5.4 mg, 0.10 mmol), **IVc** was obtained as yellow oil with 96% yield (27 mg, 0.096 mmol) as a mixture of thiol and disulfide. **^{1}H NMR (D$_2$O, 400 MHz,)** δ 4.81 (d, *J*= 3.5 Hz, 1H, *anomeric*), 3.85-3.80 (m, 2H, H-3, H-5), 3.74-3.66 (m, 2H, H-4, H-2), 3.63-3.59 (m, 3H, H-6, OC*H*$_a$CH$_2$), 3.44-3.38 (m, 1H, OC*H*$_b$CH$_2$),

[8] C.-C. Lin, Y.-C. Yeh, C.-Y. Yang, C.-L. Chen, G.-F. Chen, C.-C. Chen and Y.-C. Wu, *J. Am. Chem. Soc*. **2002**, *124*, 3508-3509.

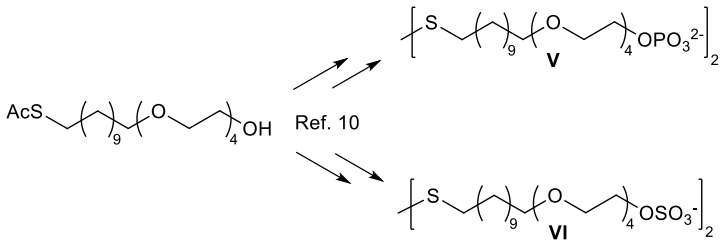
[9] O. M. Martinez-Ávila, K. Hijazi, M. Marradi, C. Clavel, C. Campion, C. Kelly and S. Penadés, *Chem. Eur. J.,* **2009***, 15,* 9874-9888.

2.65 (t, *J* = 7.0 Hz, 0.6H, C*H*$_2$SS), 2.43 (t, *J*=6.6 Hz, 1.4H, C*H*$_2$SH), 1.64-1.48 (m, 4H, OCH$_2$CH$_2$C*H*$_2$C*H*$_2$CH$_2$S), 1.39-1.31 (m, 2H, OCH$_2$C*H*$_2$CH$_2$CH$_2$CH$_2$S). **MS** (ESI) m/z (%) = calc. for $C_{22}H_{42}O_{12}S_2Na^+$ [*M*+Na]$^+$: 585.20; found: 585.29 (100%).

5-(mercapto)pentyl-α-D-mannopyranoside (IVd)[9]**:** Starting from 5-(acetylthio)pentyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside (**IIId**) (54.0 mg, 0.109 mmol) and NaOMe (5.4 mg, 0.1 mmol), **IVd** was obtained as yellow oil with 94% yield (29.0 mg, 0.103 mmol). **^{1}H NMR (CD_3OD, 200 MHz)** δ 4.73 (d, *J* = 4.0 Hz, 1H, *anomeric*), 3.84-3.39 (m, 8H, *H*-2, *H*-3, *H*-4, *H*-5, *H*-6, OC*H*$_2$), 2.70 (t, *J* = 8.0 Hz, 1.7H, C*H*$_2$SS), 2.50 (t, *J* = 8.0 Hz, 0.3H, C*H*$_2$SH), 1.75-1.46 (m, 6H, C*H*$_2$C*H*$_2$C*H*$_2$CH$_2$S).

1.2 Synthesis of anionic-ending (sulfate or phosphate) ligands

The synthesis of phosphate-ending (**V**) and sulfate-ending (**VI**) disulfide ligands was carried out following the protocols reported by Di Gianvincenzo *et al.*,[10] which started from [1-(thioacetyl)undec-11-yl]tetra(ethylene glycol) as the common precursor. Spectroscopic data obtained for **V** and **VI** are in agreement with the cited literature.



Scheme S2. *Schematic representation of ligands **V** and **VI** bearing a terminal phosphate and sulfate functionality, respectively.*

1.3 Preparation of homoligand AuNPs

1.3.1 General procedure for the preparation of AuNPs decorated with monosaccharides (glyco-AuNPs)

An aqueous solution of $HAuCl_4$ (25 mM, 1 equiv.) was added to a 12 mM methanolic solution of thiol-ending glycosides (3 equiv.). An aqueous solution of $NaBH_4$ (1 M, 27 equiv.) was then portion-wise added under magnetic stirring. The black suspension formed was stirred for 2 hours at 25 °C. After that, the supernatant was removed and analyzed by ^{1}H NMR to study the nanoparticle ligands composition. The residue was washed several times with MeOH. In order to well separate the nanoparticles from the supernatant, centrifugation (12000 rpm, 2 min) was performed. The residue was dissolved in a minimal volume of HPLC gradient grade water and purified by dialysis (SnakeSkin® Pleated Dialysis Tubing, 3500 MWCO). The glyco-AuNPs were obtained as a dark-brown powder after freeze-drying and analyzed via ^{1}H NMR, UV-Vis Spectroscopy, TEM analysis and elemental analysis. The average number of gold atoms was calculated on the basis of the average diameter obtained by TEM micrographs, which always showed gold average diameter below 2.5nm.[11] These glyco-AuNPs did not show a well-defined plasmon absorption maximum (at around 520 nm) typical of AuNPs with larger gold diameters,[12] confirming the TEM analysis. The average molecular formulas were calculated on the basis of the elemental analysis.

βGlc-Au (1)[9]**:** Starting from compound **IVa** (10.5 mg, 37.0 μmol), $HAuCl_4$ (496 μL, 25 mM) and $NaBH_4$ (335 μL, 1 M), βGlc-Au were obtained as brown powder (3.3 mg, 56% yield). **TEM** (average diameter): 1.4 ± 0.4 nm (<5% were 4.2 ± 1.2 nm); **^{1}H NMR** (400 MHz, D_2O): δ 4.43 (br signal, 1H, *anomeric*), 4.04-3.12 (br m, 8H, OC*H*$_2$-, H-2, H-3, H-4, H-5, H-6), 2.18-1.12 (br signal, 6H, 3x -C*H*$_2$-); **UV-Vis** (H_2O, 0.2 mg/mL): no SPR peak observed; **Elemental analysis** found (%): C 22.28, H 3.67, S 5.02; calc. for $Au_{201}(C_{11}H_{21}O_6S)_{124}$: C 22.00, H 3.52, S 5.34; average molecular weight: 74 kDa.

βGal-Au (2)[7]**:** Starting from compound **IVb** (10.0 mg, 35.4 μmol), $HAuCl_4$ (472 μL, 25 mM) and $NaBH_4$ (319 μL, 1 M), βGal-Au were obtained as brown powder (3.0 mg, 53% yield). **TEM** (average diameter): 1.3 ± 0.3 nm; **^{1}H NMR** (400 MHz, D_2O):

[10] P. Di Gianvincenzo, M. Marradi, O. M. Martínez-Ávila, L. M. Bedoya, J. Alcamí, S. Penadés, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 2718-2721.

[11] M. J. Hostetler, J. E. Wingate, C.-J. Zhong, J. E. Harris, R. W. Vachet, M. R. Clark, J. D. Londono, S. J. Green, J. J. Stokes, G. D. Wignall, G. L. Glish, M. D. Porter, N. D. Evans, R. W. Murray, *Langmuir* **1998**, *14*, 17-30.

[12] M. Zhou, C. Zeng, Y. Chen, S. Zhao, M. Y. Sfeir, M. Zhu and R. Jin, *Nat. Commun*. **2016**, *7*, 1-7.

δ 4.38 (br signal, 1H, *anomeric*), 4.12-3.42 (br m, 8H, OC*H*$_2$-, H-2, H-3, H-4, H-5, H-6), 2.17-1.41 (br m, 6H, 3x -C*H*$_2$-); **UV-Vis** (H_2O, 0.1 mg/mL): no SPR peak observed; **Elemental analysis** found (%): C 16.60, H 2.61, S 4.57; calc. for $Au_{140}(C_{11}H_{21}O_6S)_{53}$: C 16.48, H 2.64, S 4.00; average molecular weight: 42 kDa.

αGal-Au (3): Starting from compound **IVc** (7.0 mg, 24.8 µmol), $HAuCl_4$ (330 µL, 25 mM) and $NaBH_4$ (223 µL, 1 M), αGal-Au were obtained as brown powder (1.8 mg, 46% yield). **TEM** (average diameter): 2.0 ± 0.5 nm; **^{1}H NMR** (400 MHz, D_2O): δ Anomeric proton presumably hidden under HDO/H_2O signal; 4.22-3.26 (br m, 8H, OC*H*$_2$-, H-2, H-3, H-4, H-5, H-6), 2.30-1.32 (br m, 6H, 3x -C*H*$_2$-); **UV-Vis** (H_2O, 0.1 mg/mL): no SPR peak observed; **Elemental analysis** found (%): C 18.01, H 3.04, S 4.53; calc. for $Au_{201}(C_{11}H_{21}O_6S)_{90}$: C 18.32, H 2.93, S 4.45; average molecular weight: 65 kDa.

αMan-Au (4)[9]**:** Starting from compound **IVd** (7.6 mg, 27.0 µmol), $HAuCl_4$ (360 µL, 25 mM) and $NaBH_4$ (243 µL, 1 M), αMan-Au were obtained as brown powder (2.2 mg, 92% yield). **TEM** (average diameter): 2.0 ± 0.4 nm; **^{1}H NMR** (400 MHz, D_2O): δ Anomeric proton presumably hidden under HDO/H_2O signal; 3.89-3.49 (br m, 8H, OC*H*$_2$-, H-2, H-3, H-4, H-5, H-6), 1.89-1.02 (br m, 6H, 3x -C*H*$_2$-).; **UV-Vis** (H_2O, 0.1 mg/mL): no SPR peak observed; **Elemental analysis** found (%): C 19.12, H 3.17, S 5.00; calc. for $Au_{201}(C_{11}H_{21}O_6S)_{97}$: C 19.16, H 3.07, S 4.65; average molecular weight: 69 kDa.

1.3.2 General Procedure for the preparation of AuNPs coated with phosphated or sulfated ligands

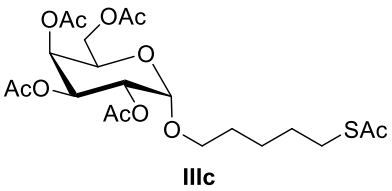
An aqueous solution of $HAuCl_4$ (25 mM, 1 equiv.) was added to a suitable mixture of thiol-ending sugar and phosphated or sulfated ligands (3 equiv. overall) in MeOH/H_2O/CH_3COOH (3:3:1). An aqueous solution of $NaBH_4$ (1 M, 27 equiv.) was then portion-wise added under magnetic stirring. The black suspension formed was stirred for 2 hours at 25 °C. The solvent was evaporated at reduced pressure. The residue was washed several times with EtOH. In order to well separate the nanoparticles from the supernatant a centrifugation (12000 rpm, 2 min) was performed. The supernatant was removed and analysed by ^{1}H NMR to study the nanoparticle ligands composition. The residue was dissolved in a minimal volume of HPLC Gradient grade water and purified by dialysis (SnakeSkin® Pleated Dialysis Tubing, 3500 MWCO). The Au-NPs were obtained as a dark-brown powder after freeze-drying and characterized via ^{1}H NMR, UV-Vis Spectroscopy, TEM analysis and elemental analysis. The average number of gold atoms was calculated on the basis of the average diameter obtained by TEM micrographs.

Au-OSO_3^- (5)[10]**:** Starting from compound **VI** (15.3 mg, 15.9 mmol), $HAuCl_4$ (211 µL, 25 mM) and $NaBH_4$ (117 µL, 1 M), Au-OSO_3^- **5** were obtained as brown amorphous powder (3.0 mg). **TEM** (average diameter): 1.9 ± 0.3 nm; **^{1}H NMR** (400 MHz, D_2O): δ 4.14 (br signal, 2H, -C*H*$_2$$OSO_3$), 3.82-3.36 (br m, 16H, 3x -OC*H*$_2$C*H*$_2$O-, 2x -OCH_2-), 1.71-1.14 (br m, 18H, 9x -C*H*$_2$-); **UV-Vis** (H_2O, 0.1 mg/mL): no SPR peak observed; **Elemental analysis** found (%): C 25.69, H 4.39, S 7.62; calc. for $Au_{201}(C_{19}H_{38}O_8S_2Na)_{98}$: C 25.77, H 4.32, S 7.24; average molecular weight: 87 kDa.

Au-OPO_3^{2-} (6)[10]**:** Starting from compound **V** (16.8 mg, 34.8 µmol), $HAuCl_4$ (232 µL, 25 mM) and $NaBH_4$ (157 µL, 1 M), Au-OPO_3^{2-} **6** was obtained as brown powder (2.5 mg). **TEM** (average diameter): 2.3 ± 0.5 nm; **^{1}H NMR** (400 MHz, D_2O): δ 3.94 (br signal, 2H, -C*H*$_2$$OPO_3^{2-}$), 3.77-3.50 (br m, 16H, 3x -OC*H*$_2$C*H*$_2$O-, 2x -OC*H*$_2$-), 1.68-1.18 (br m, 18H, 9x -C*H*$_2$-); **UV-Vis** (H_2O, 0.1 mg/mL): no SPR peak observed; **Elemental analysis** found (%): C 25.38, H 4.29, S 3.90; calc. for $Au_{201}(C_{19}H_{39}O_8PSNa)_{95}$: C 25.40, H 4.38, S 3.57; average molecular weight: 85 kDa.

2. Characterization of Selected Products

2.1 NMR spectra for compounds IIIc (^{1}H and ^{13}C NMR) and IVc (^{1}H NMR)



IIIc

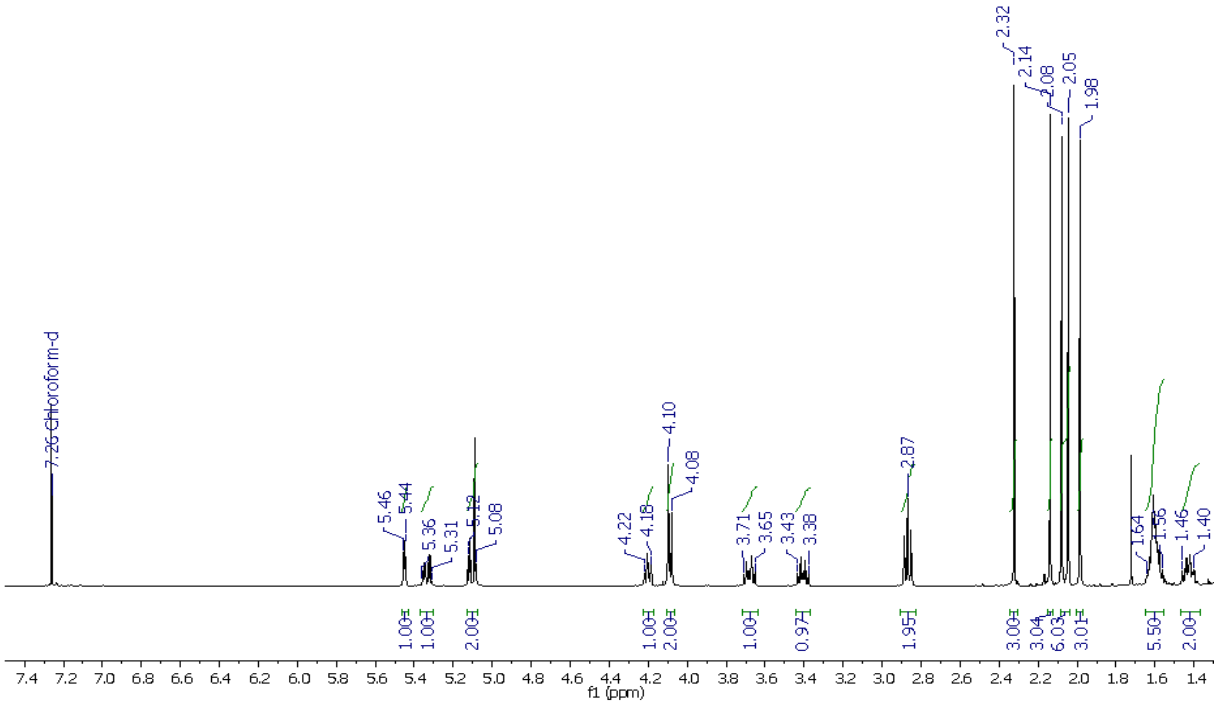


Figure S1. *^{1}H NMR spectrum of compound **IIIc** (400 MHz, $CDCl_3$).*

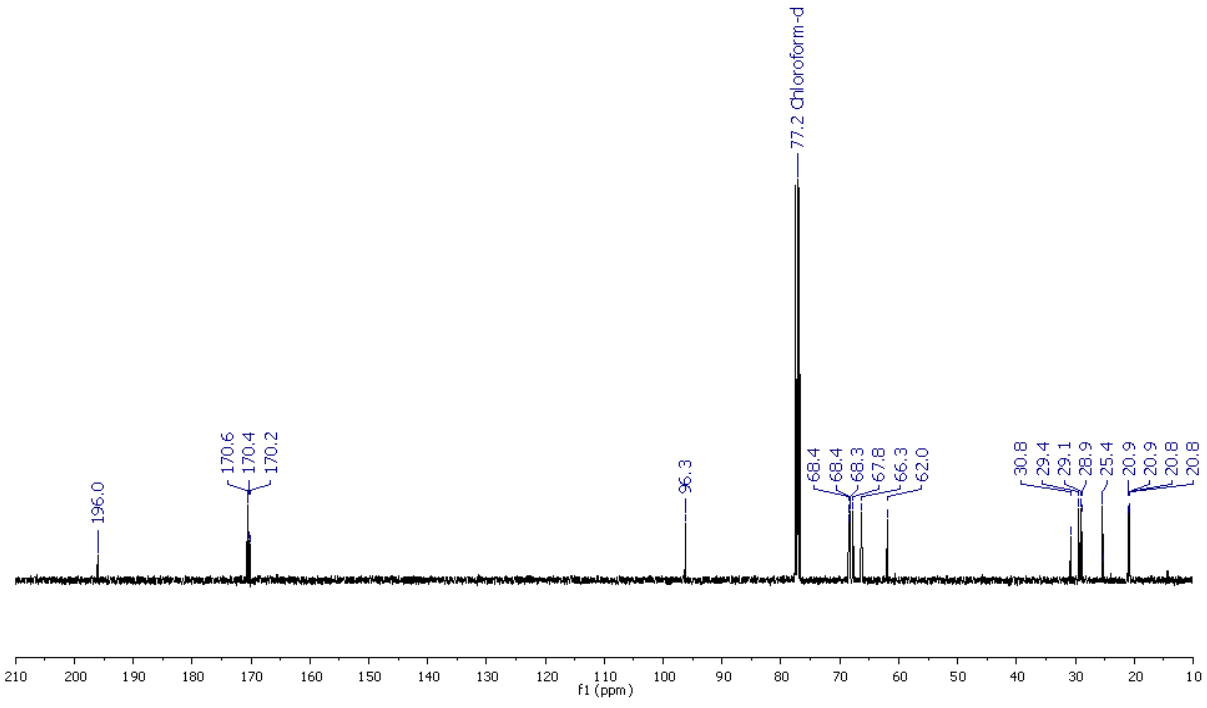


Figure S2. *^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **IIIc**.*

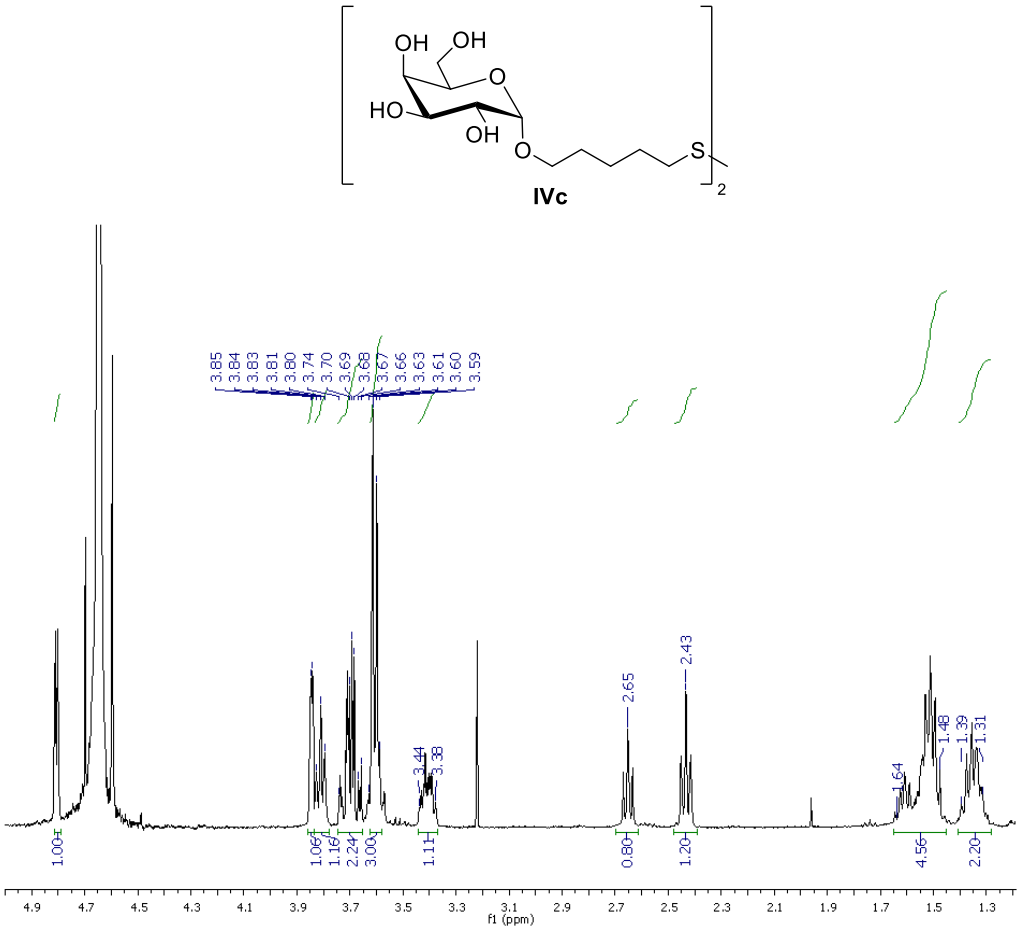


Figure S3. *^{1}H NMR (400 MHz, D_2O) spectrum of compound **IVc**.*

2.2 ^{1}H NMR and TEM of AuNPs

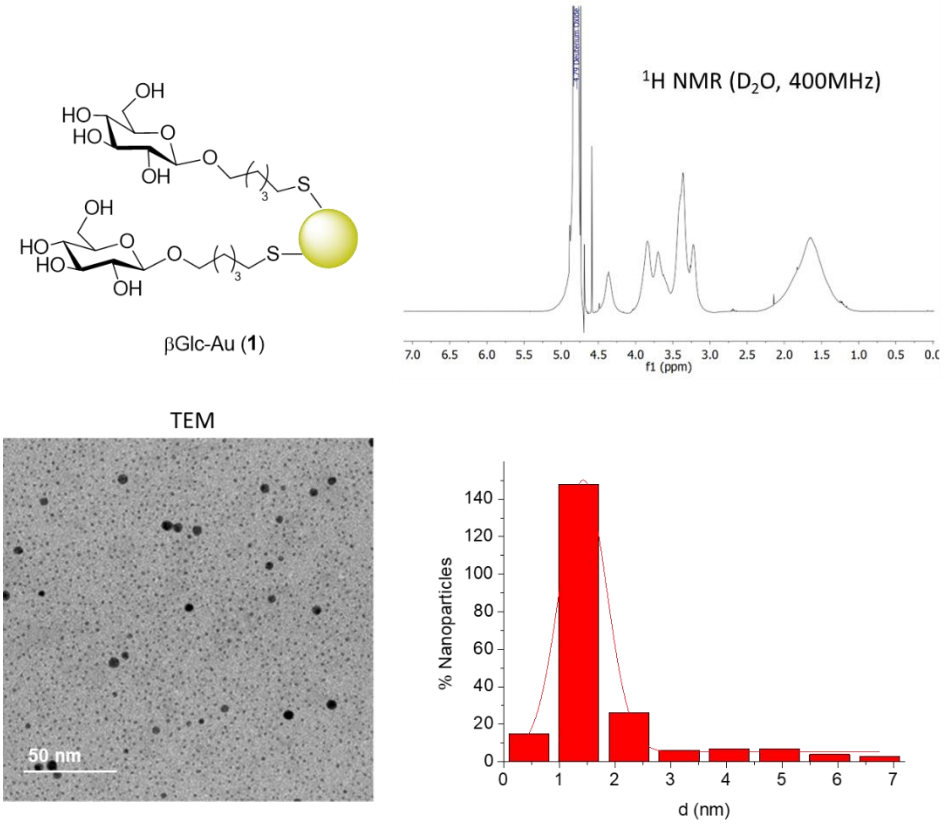


Figure S4. *Characterization of glyco-AuNPs **1***

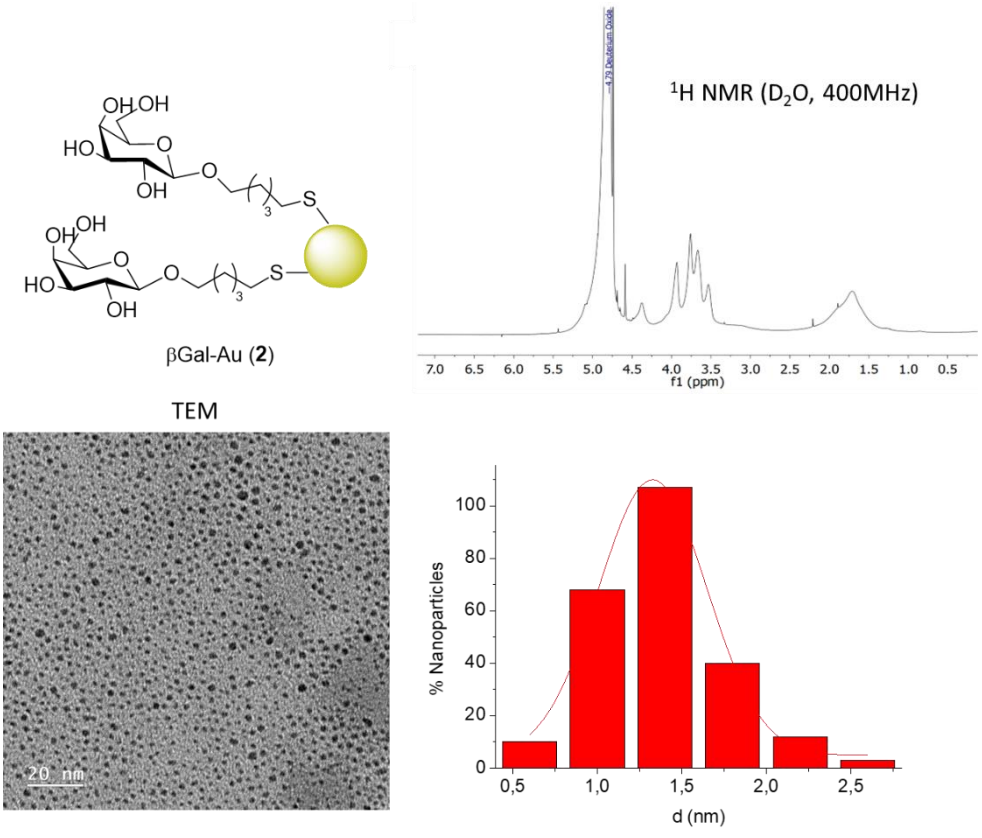


Figure S5. *Characterization of glyco-AuNPs **2***

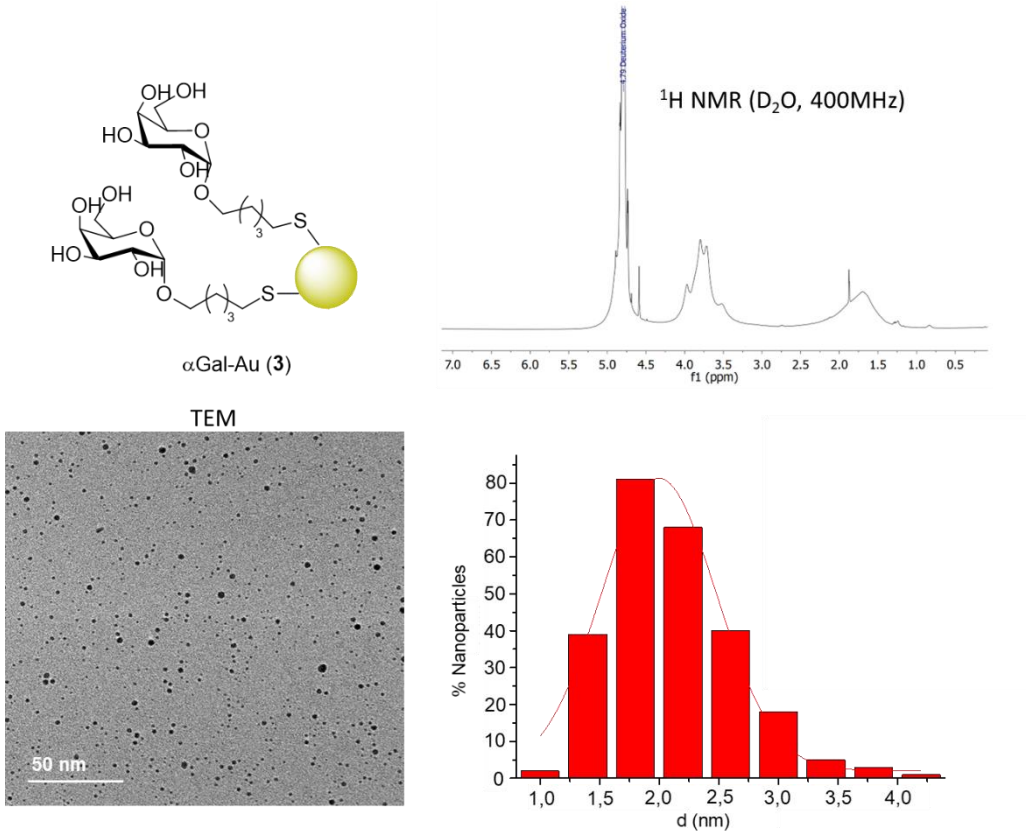


Figure S6. *Characterization of glyco-AuNPs* ***3***

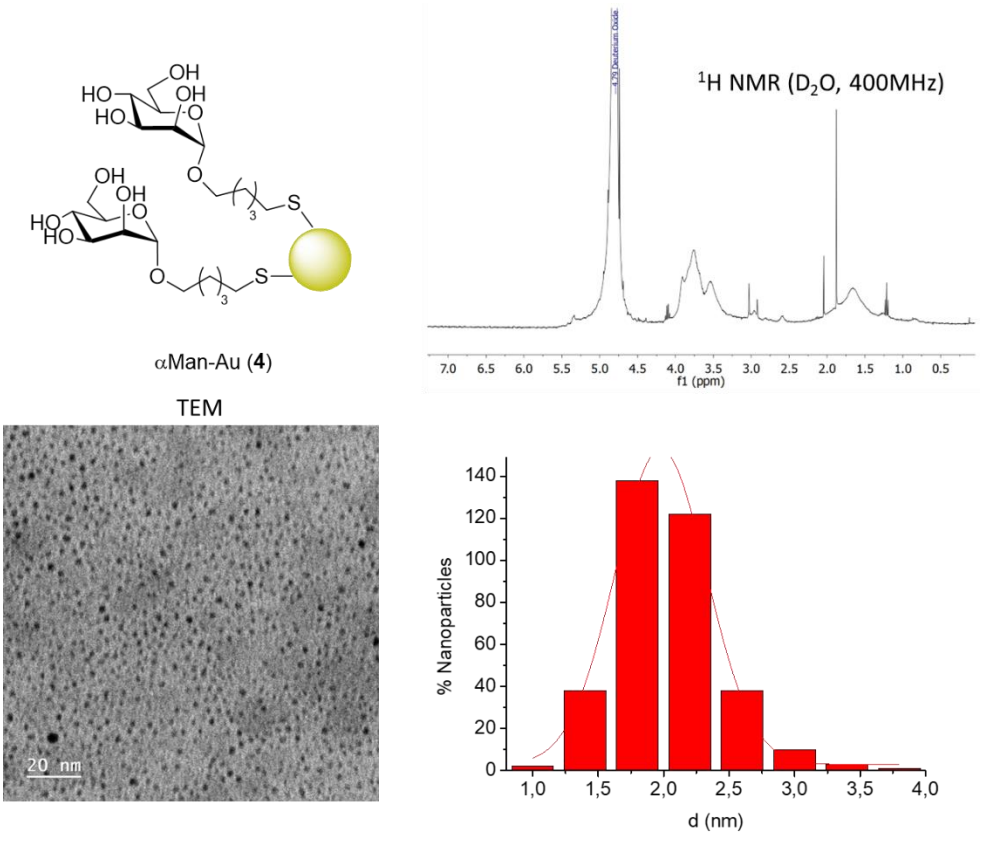


Figure S7. *Characterization of glyco-AuNPs* ***4***

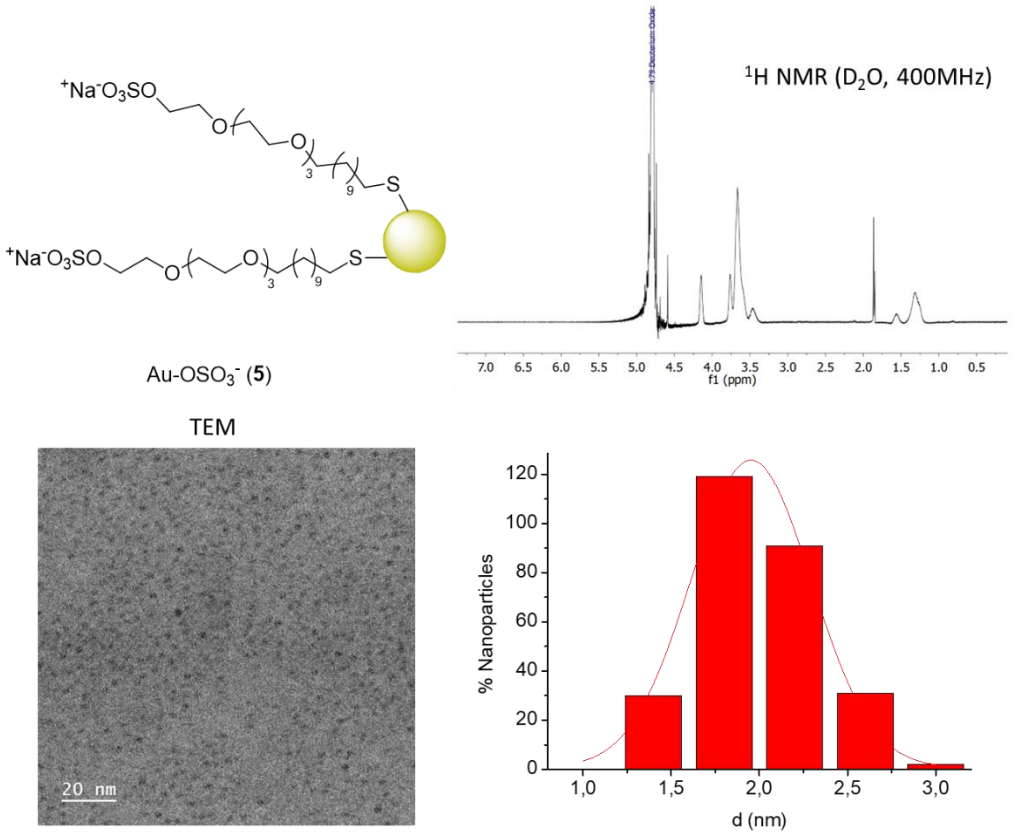


Figure S8. *Characterization of AuNPs **5***

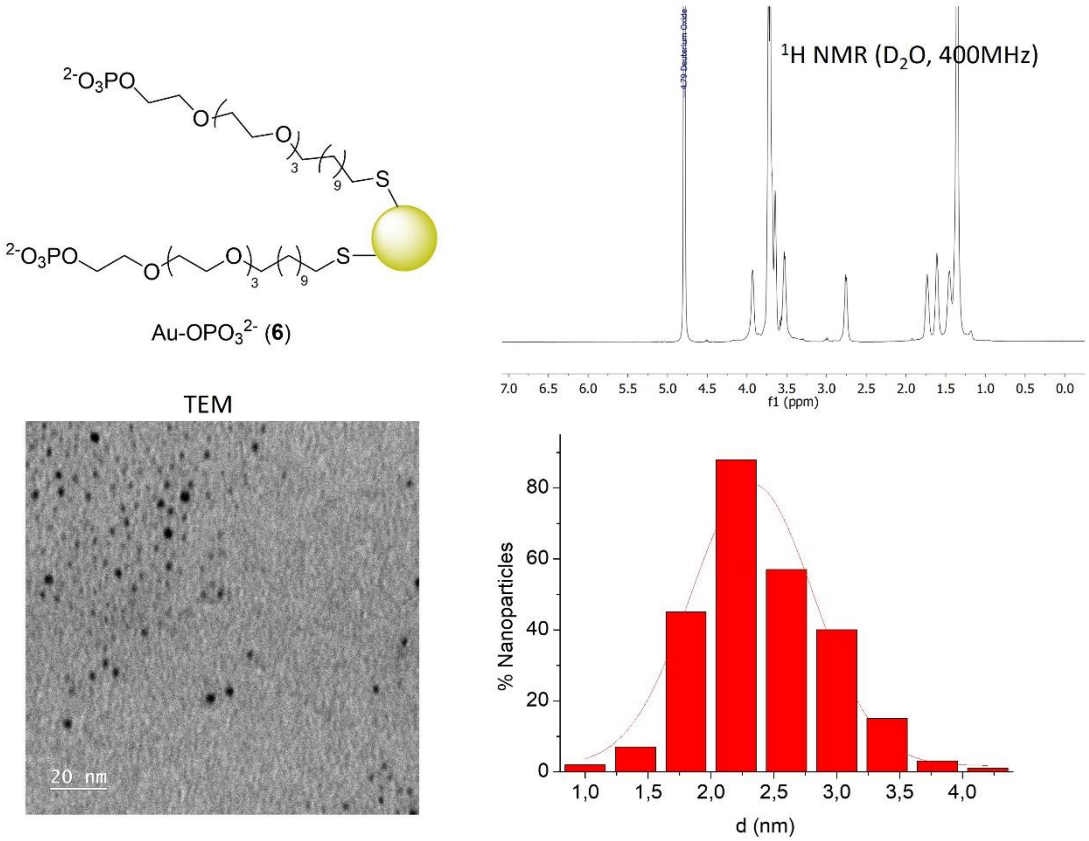


Figure S9. *Characterization of AuNPs **6***

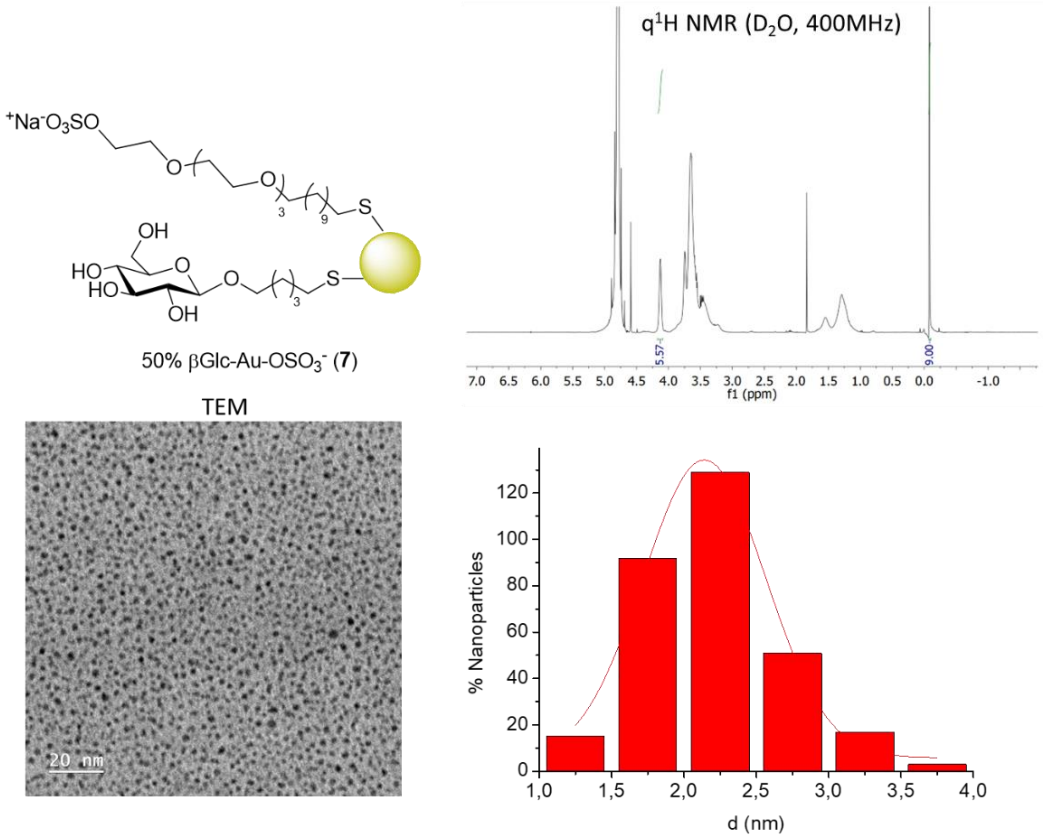


Figure S10. *Characterization of AuNPs* ***7***

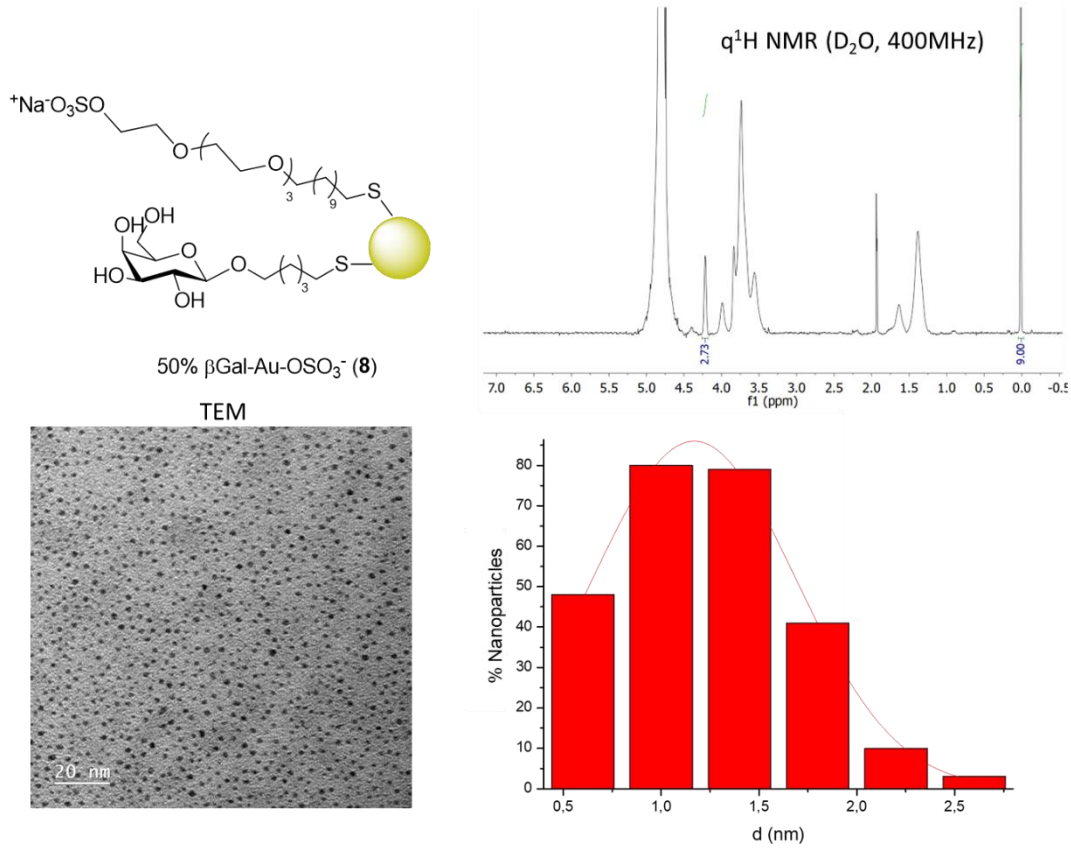


Figure S11. *Characterization of AuNPs* ***8***

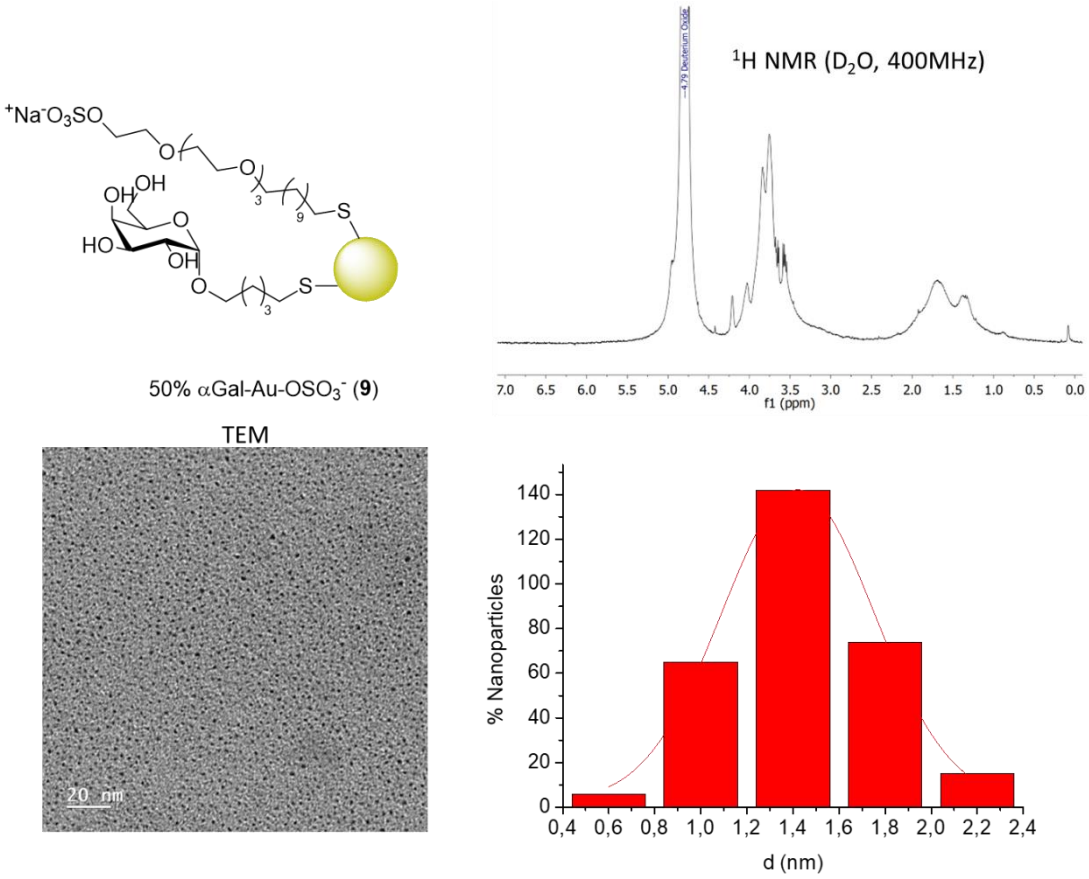


Figure S12. *Characterization of AuNPs **9***

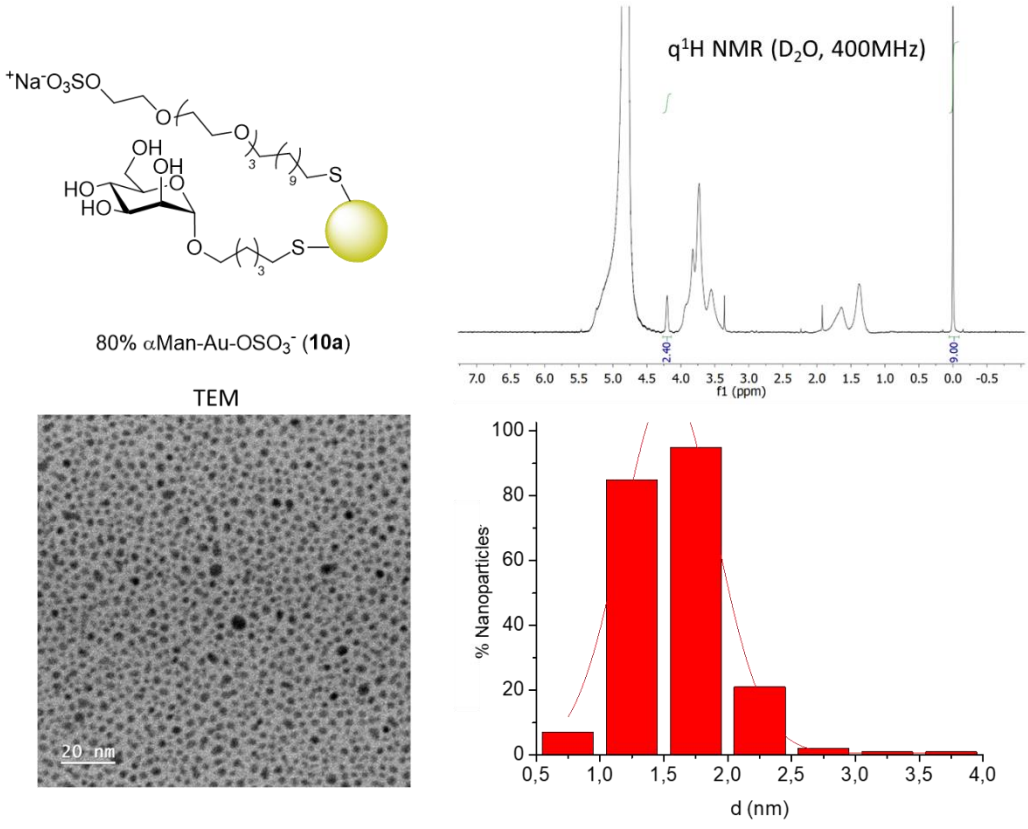


Figure S13. *Characterization of AuNPs **10a***

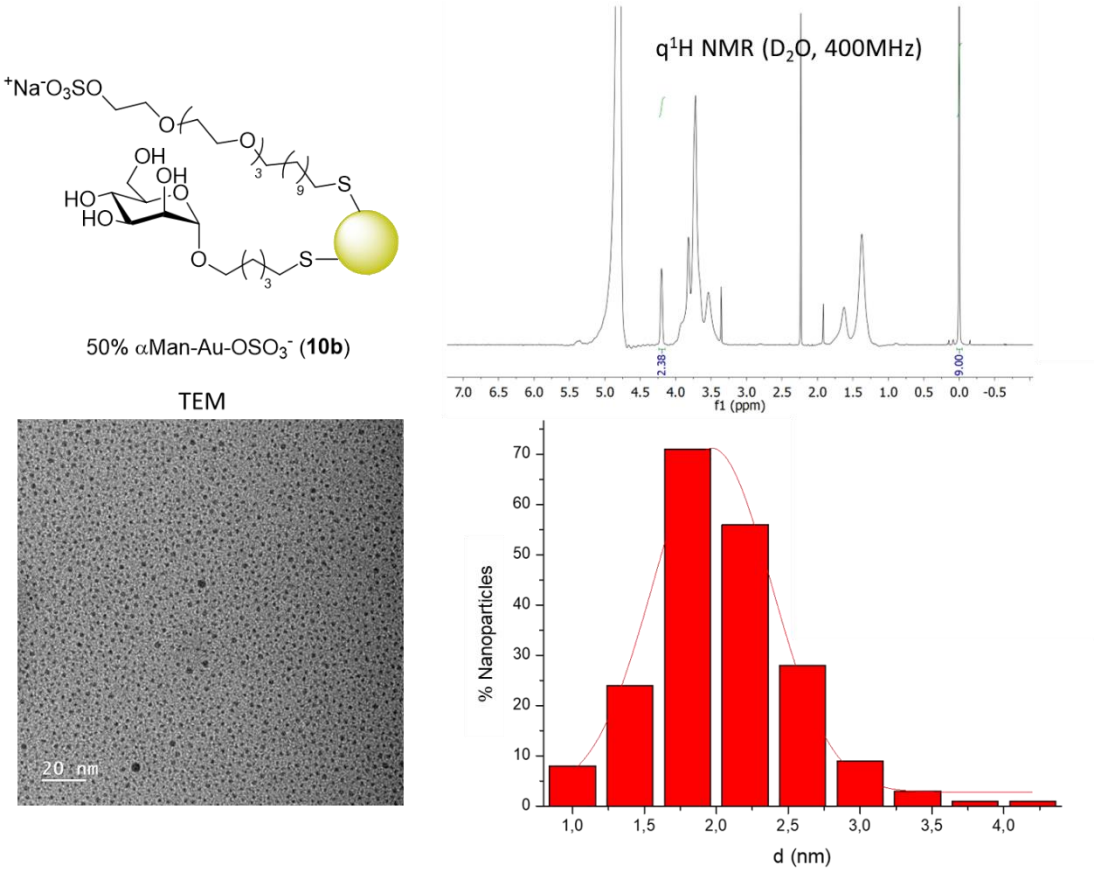


Figure S14. *Characterization of AuNPs **10b***

Table S1. *Main properties of the prepared AuNPs*

AuNP	Mean Au core diameter (nm)[a]	Average number of Au atoms[b]	Elemental Analysis (% found)[c]	Estimated average molecular formula[d] and corresponding elemental analysis (% calculated)	Estimated average molecular weight (kDa)
1	1.4 ± 0.4 (<5% 4.2 ± 1.2)	201	C 22.28, H 3.67, S 5.02	$Au_{201}(C_{11}H_{21}O_6S)_{124}$ C 22.00, H 3.52, S 5.34	74
2	1.3 ± 0.3	140	C 16.60, H 2.61, S 4.57	$Au_{140}(C_{11}H_{21}O_6S)_{53}$ C 16.48, H 2.64, S 4.00	42
3	2.0 ± 0.5	201	C 18.01, H 3.04, S 4.53	$Au_{201}(C_{11}H_{21}O_6S)_{90}$ C 18.32, H 2.93, S 4.45	65
4	2.0 ± 0.4	201	C 19.12, H 3.17, S 5.00	$Au_{201}(C_{11}H_{21}O_6S)_{97}$ C 19.16, H 3.07, S 4.65	69
5	1.9 ± 0.3	201	C 25.69, H 4.39, S 7.62	$Au_{201}(C_{19}H_{38}O_8S_2Na)_{98}$ C 25.77, H 4.32, S 7.24	87
6	2.3 ± 0.5	201	C 25.38, H 4.29, S 3.90	$Au_{201}(C_{19}H_{39}O_8PSNa)_{95}$ C 25.40, H 4.38, S 3.57	85
7	2.2 ± 0.4	201	C 25.32, H 4.54, S 6.34	$Au_{201}(C_{19}H_{38}O_8S_2Na)_{60}(C_{11}H_{21}O_6S)_{60}$ C 25.32, H 4.18, S 6.76	85
8	1.2 ± 0.4	140	C 13.91, H 2.18, S 3.41	$Au_{140}(C_{19}H_{38}O_8S_2Na)_{15}(C_{11}H_{21}O_6S)_{15}$ C 13.85, H 2.29, S 3.70	39
9	1.4 ± 0.3	140	C 25.32, H 4.54, S 6.34	$Au_{140}(C_{19}H_{38}O_8S_2Na)_{41}(C_{11}H_{21}O_6S)_{41}$ C 25.10, H 4.14, S 6.70	58
10a	1.5 ± 0.4	140	C 17.31, H 2.78, S 4.63	$Au_{140}(C_{19}H_{38}NaO_8S_2)_{10}(C_{11}H_{21}O_6S)_{40}$ C 17.34, H 2.82, S 4.41	44
10b	2.0 ± 0.4	201	C 17.34, H 2.92, S 4.93	$Au_{201}(C_{11}H_{21}O_6S)_{30}(C_{19}H_{38}O_8S_2Na)_{30}$ C 17.30, H 2.86, S 4.62	62

[a]Diameter of the gold nanocluster (as measured by TEM); [b]The average number of gold atoms per nanoparticle was calculated from the size of the gold cluster obtained by TEM, as reported previously[11]; [c]Experimental values of elemental analysis obtained in terms of elements percentage; [d]Average molecular formula estimated by combining TEM[11] and the values of the elemental analysis found.

3. Biological Evaluation

3.1 Enzymatic assays towards human GALNS in leukocytes isolated from healthy donors

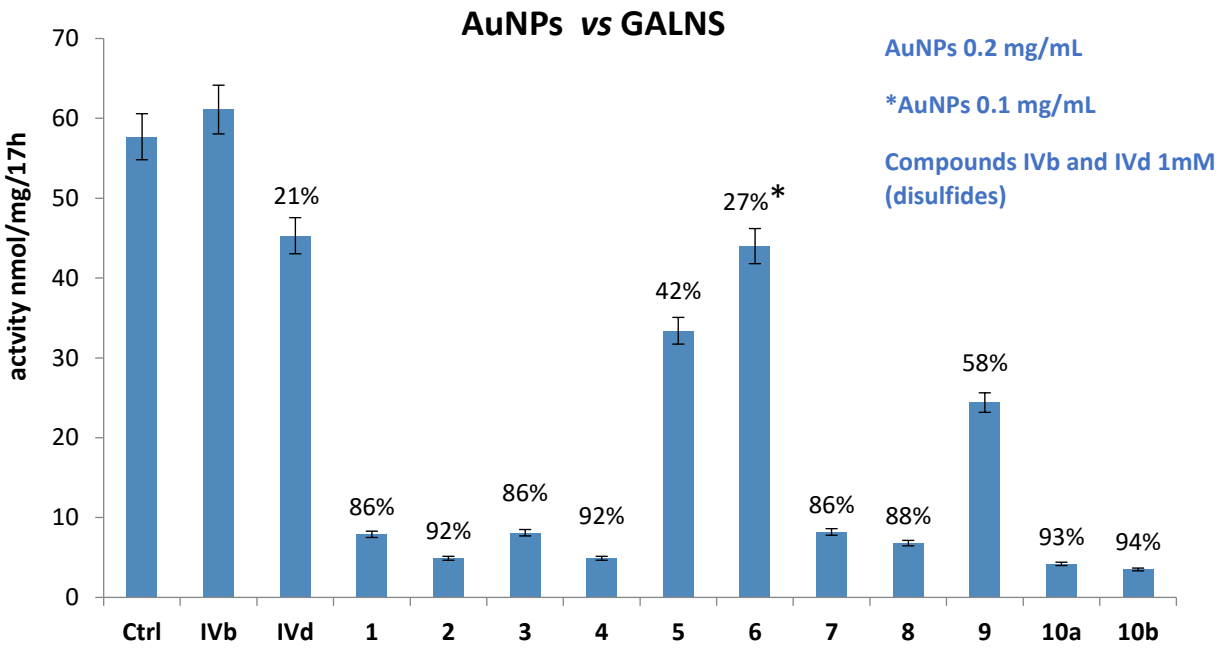
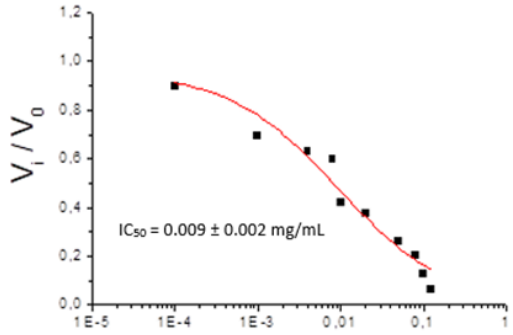


Figure S15. *Activity of GALNS in the absence (Ctrl) and presence of compounds **IVb** and **IVd** at 1mM, AuNPs **1**-**5** and **7**-**10** at 0.2 mg/mL and AuNPs **6** at 0.1 mg/mL in human leukocytes extracts. The corresponding calculated percentage of inhibition is indicated above each bar.*

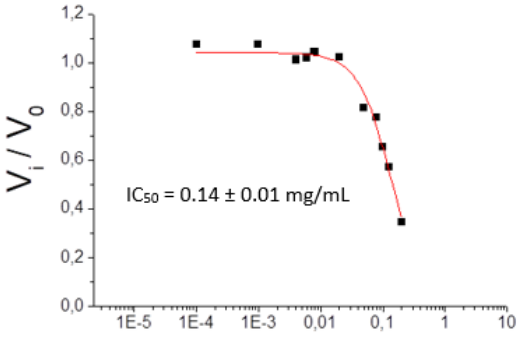
IC_{50} determination: The IC_{50} values of inhibitors against GALNS in leukocyte homogenate were determined by measuring the initial hydrolysis rate with 4-methylumbelliferyl-β-galactoside-6-sulfate·Na (6.66 mM) at different concentrations of AuNPs (concentration range from 10^{-4} mg/mL to 0.2 mg/mL). Data obtained were fitted to the following equation using the OriginPro 2021 (Version 2021. OriginLab Corporation, Northampton, MA, USA):

$$\frac{Vi}{Vo} = \frac{Max - Min}{1 + \left(\frac{x}{IC_{50}}\right)^{slope}} + Min$$

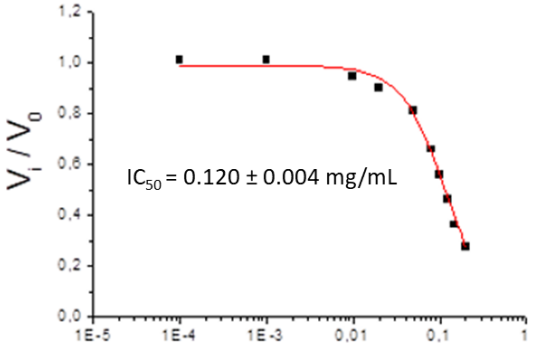
where V_i/V_o, represent the ratio between the activity measured in the presence of the inhibitor (V_i) and the activity of the control without the inhibitor (V_o), "x" the inhibitor concentration, Max and Min, the maximal and minimal enzymatic activity observed, respectively.



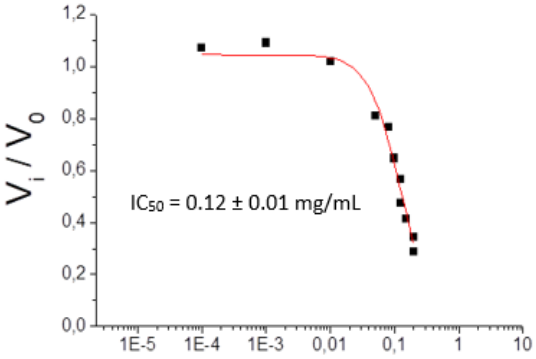
AuNPs **2** [mg/mL]



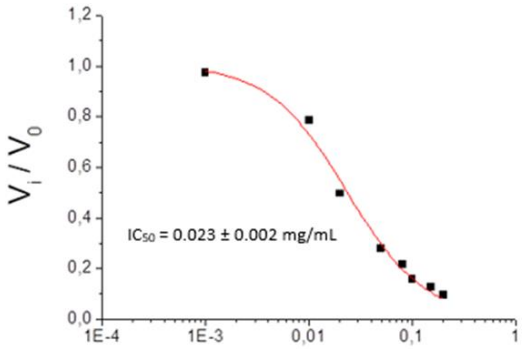
AuNPs **3** [mg/mL]



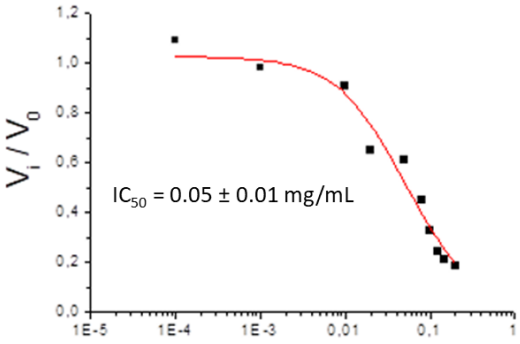
AuNPs **4** [mg/mL]



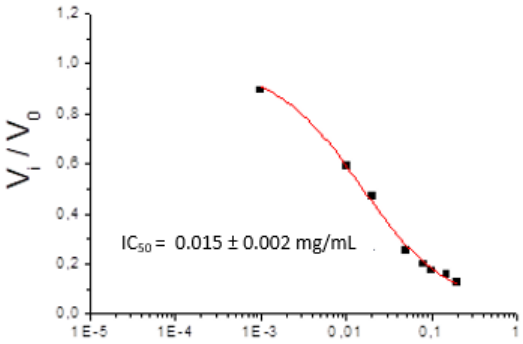
AuNPs **7** [mg/mL]



AuNPs **8** [mg/mL]



AuNPs **10a** [mg/mL]



AuNPs **10b** [mg/mL]

Figure S16. *IC_{50} curves of AuNPs **2-4**, **7**, **8**, **10a** and **10b** in human leukocyte homogenates from healthy donors.*

3.2 Enzymatic assays towards recombinant human GALNS (rhGALNS VIMIZIM®)

IC_{50} determination of AuNPs 2: the IC_{50} value of AuNPs **2** against recombinant human GALNS (rhGALNS VIMIZIM®) was determined by measuring the initial hydrolysis rate with 4-methylumbelliferyl-β-galactoside-6-sulfate·Na (6.66 mM) at different concentrations of AuNPs **2**. For the assay the recombinant enzyme was diluted in bovine serum albumin (0.2%) at final concentration of $1*10^{-5}$ mg/mL.

AuNPs **2** solution (3 µL) (concentration range from 10^{-4} mg/mL to 0.2 mg/mL), rhGALNS VIMIZIM® and 20 µL of 4-methylumbelliferyl-β-galactoside-6-sulfate·Na substrate solution (6.66mM) in Na-Acetate/acetic acid buffer (0.1 M/0.1 M, pH 4.3) containing 0.1 M NaCl , 0.02% (w/v) NaN_3 and 5 mM Pb-acetate were incubated for 17 h at 37 °C. After this incubation, the tubes were placed on an ice cooler and the reaction was stopped by addition of 5 µL of Na-phosphate buffer (0.9 M, pH 4.3) containing 0.02% (w/v) of NaN_3 and by efficient mixing with vortex. Then, 10 µL of β-Gal-A-10U were added to each sample and samples were incubated for 2 h at 37°C. After this time, the tubes were placed on an ice cooler and the samples were transferred in a cooled flat–bottomed 96 well plate and the reaction was immediately stopped with 200 µL of $NaHCO_3/Na_2CO_3$ buffer (0.5 M/0.5 M pH 10.7) containing 0.025% (w/v) of Triton X-100. Fluorescence was measured in a SpectraMax M2 microplate reader (Molecular-Devices) using a 365 nm excitation wavelength and a 435 nm emission wavelength. Experiments were performed in triplicate, and the mean ± S. D. was calculated. Data obtained were fitted to the above reported equation using the Origin Microcal program.

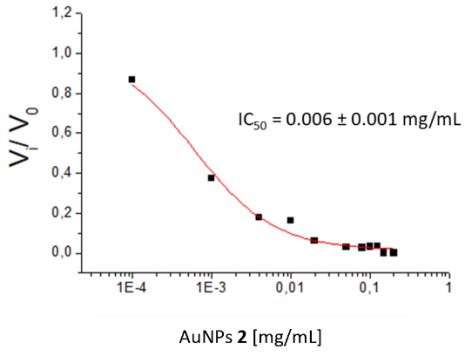


Figure S17. *IC_{50} curve of AuNPs **2** towards recombinant human GALNS (rhGALNS VIMIZIM®).*

Kinetic Analysis for AuNPs 2: the action mechanism of AuNPs **2** was determined by studying the dependence of the main kinetic parameters (K_m and V_{max}) from the inhibitor concentration (Figure S18 and Figure S19). The rhGALNS VIMIZIM® activity was determined using the 4-methylumbelliferyl-β-galactoside-6-sulfate·Na as the substrate (at different concentrations), in absence (0 µg/mL) or in presence (0.5 µg/mL, 1.0 µg/mL, 2.0 0 µg/mL final concentrations) of AuNPs **2**. The enzyme was diluted in bovine serum albumin (0.2%) at final concentration of $1*10^{-5}$ mg/mL. The enzyme activity was determined with the same protocol reported above for the IC_{50} determination.

Kinetic data were analysed using the Lineweaver-Burk plot. Following the equation for the non-competitive inhibition, the Ki value for AuNPs **2** was calculated (0.76 ± 0.01 µg/mL), as reported in Figure S20.

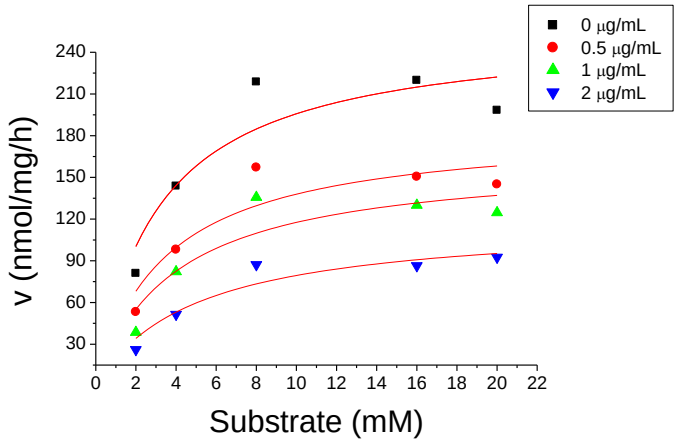


Figure S18. *Fitting of the data obtained using increasing concentrations of the AuNPs **2**. The experimental data were fitted using the Michaelis-Menten equation. The symbols shown in the figure represent the different concentrations of AuNPs **2**: 0 µg/mL; 0.5 µg/mL; 1 µg/mL; 2 µg/mL. Data reported in the figures represent the mean values ± S.E.M. (n = 3).*

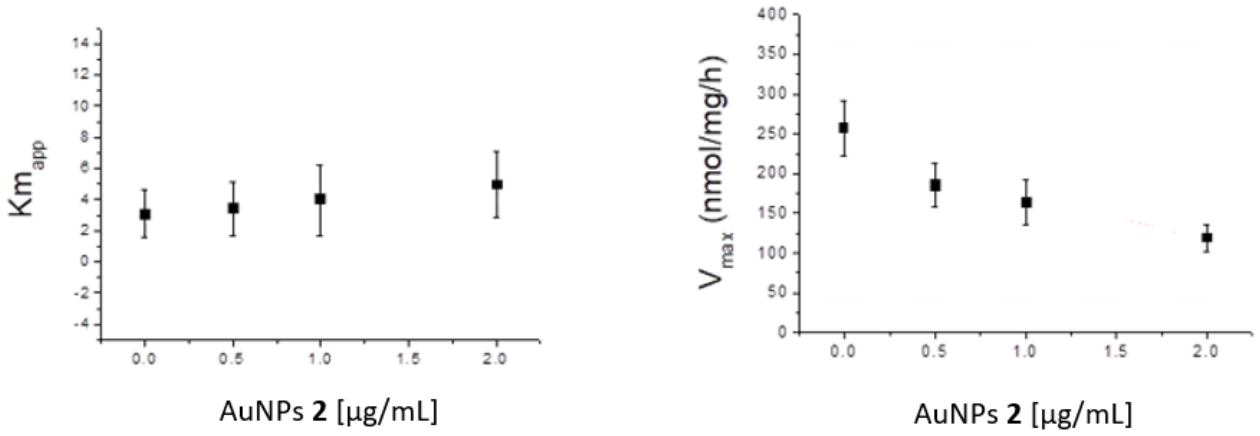


Figure S19. *Behaviour of K_m and V_{max} at different concentrations of AuNPs **2**.*

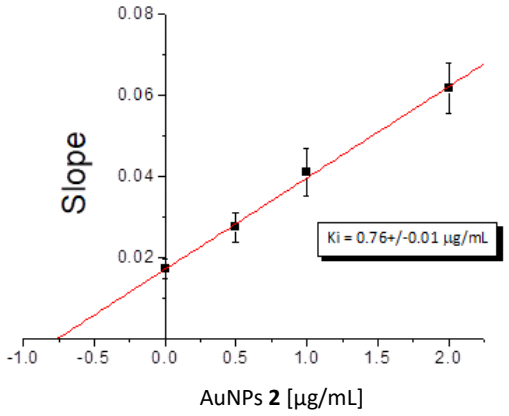


Figure S20. *Plot for the determination of the Ki value of AuNPs **2**.*

3.3 Stabilization of Recombinant GALNS under Thermal Denaturation Conditions[13]

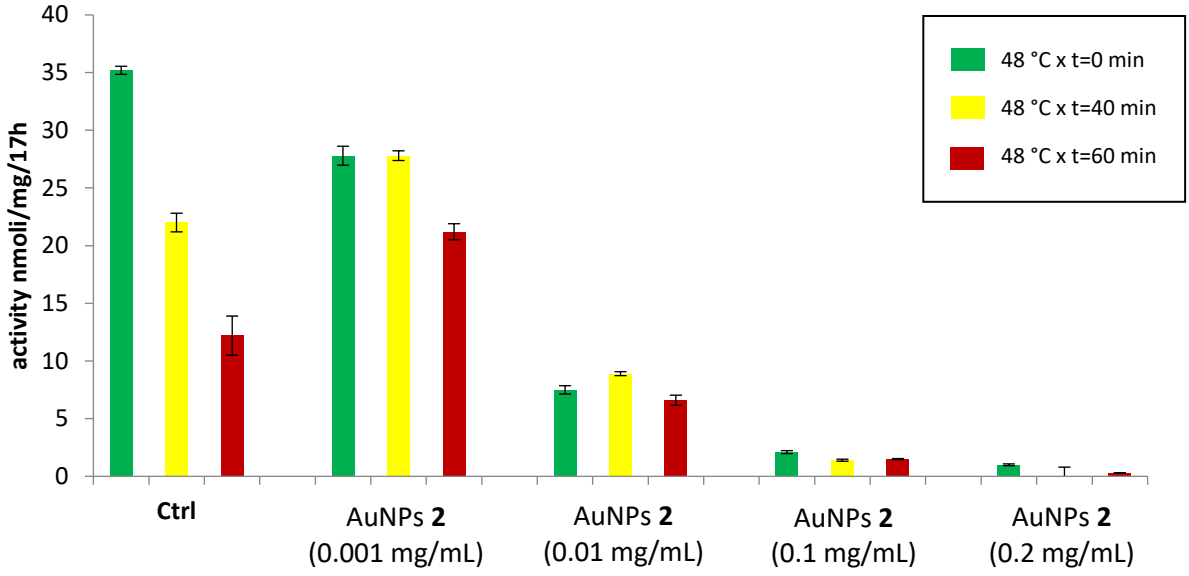


Figure S21. *Activity of recombinant human GALNS (rhGALNS VIMIZIM®) was determined after incubation for 0 minutes or 40 minutes or 60 minutes at 48 °C with or without (Ctrl) different concentrations of AuNPs* ***2*** *by measuring the hydrolysis rate with 4-methylumbelliferyl-ß-galactoside-6-sulfate·Na.*

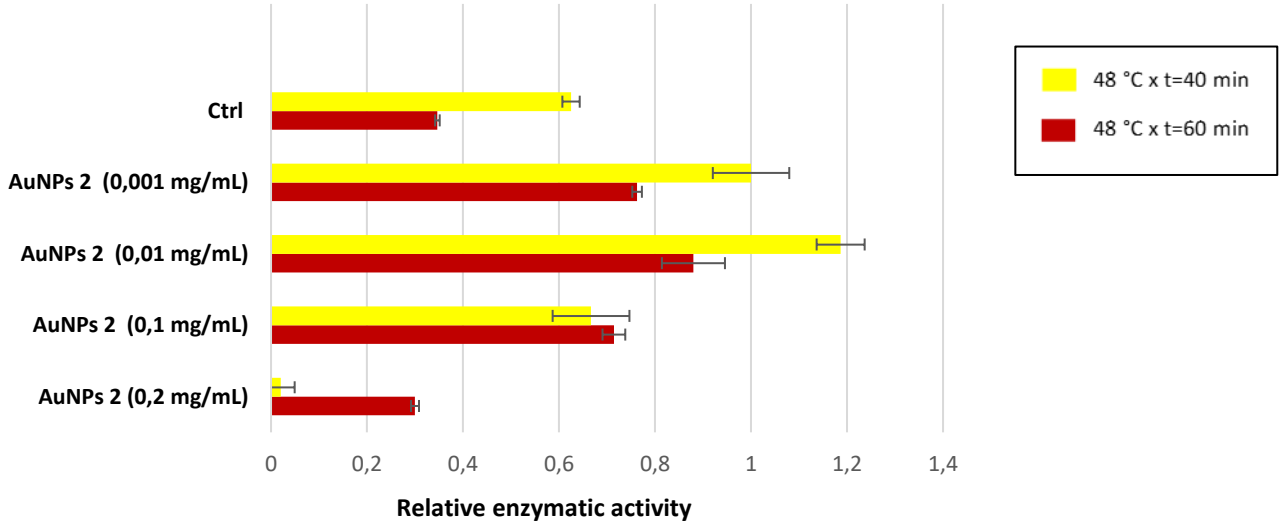


Figure S22. *Relative enzymatic activity (the ratio of relative enzymatic activities inhibitor* vs *control at 37 °C) after thermal denaturation (48 °C) for 40 min and 60 min at the indicated inhibitor concentrations (mg/mL) compared to the corresponding assay at 37 °C. Data for control are obtained as above except that no inhibitor is present (Ctrl).*

[13] a) R. Sawkar, W. C. Cheng, E. Beutler, C. H. Wong, W. E. Balch and J. W. Kelly, *Proc. Natl. Acad. Sci. U.S.A.,* **2002**, *99*, 15428. b) A. Trapero, I. Alfonso, T. D. Butters, A. Llebaria, *J. Am. Chem. Soc.* **2011**, *133*, 5474. c) M.Egido-Gabàs, D. Canals, J. Casas, A. Llebaria, A. Delgado, *ChemMedChem* **2007**, *2*, 992.

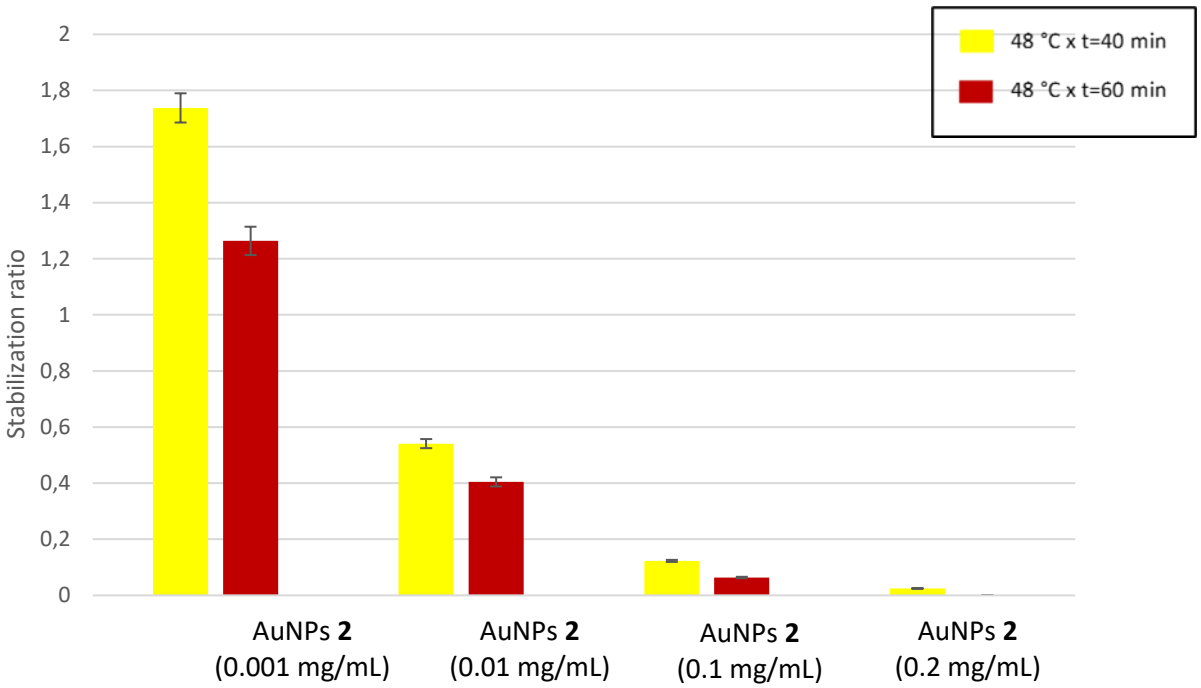


Figure S23. *Stabilization ratio (the ratio of relative enzymatic activities inhibitor vs control) after thermal denaturation (48 °C) for 40 and 60 min at the indicated inhibitor concentrations (mg/mL). Enzyme activity is reported relative to unheated enzyme.*