Supplementary Information

Second generation of Fucose-based DC-SIGN ligands : affinity improvement and specificity *versus* Langerin

Manuel Andreini[a] §, Daniela Doknic[a] §, Ieva Sutkeviciute[b], [e] §, José J. Reina[a], Janxin Duan[c], Eric Chabrol[b], [e], Michel Thepaut[b], [e], [f], Elisabetta Moroni[a], Fabio Doro[a], Laura Belvisi[a], Joerg Weiser[c], Javier Rojo[d], Franck Fieschi*[b], [e], [g], Anna Bernardi*[a]

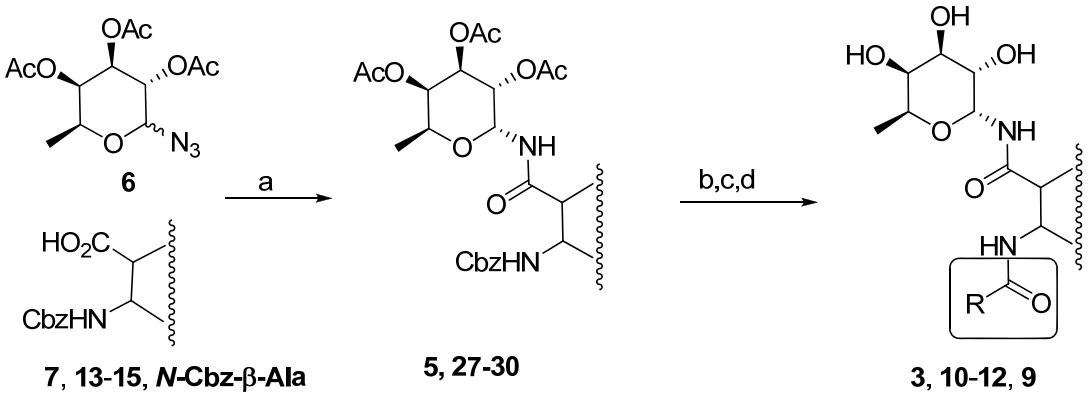
§ these authors, listed in alphabetical order, contributed equally to this work

a) Universita' degli Studi di Milano, Dipartimento di Chimica Organica e Industriale and CISI, via Venezian 21, 20133 Milano, Italy, anna.bernardi@unimi.it
b) Institut de Biologie Structurale, Université Grenoble I, 41 rue Jules Horowitz, 38027 Grenoble, France, fieschi@ibs.fr
c) Anterio consult&research, Augustaanlage 23, D-68165 Mannheim, Germany
d) Glycosystems Laboratory, Instituto de Investigaciones Químicas, CSIC – Universidad de Sevilla, Américo Vespucio 49, 41092 Sevilla (Spain)
e) CNRS, UMR 5075, Grenoble, France
f) CEA, Grenoble, France
g) Institut Universitaire de France, 103 boulevard Saint-Michel 75005 Paris, France

Supplementary Information

1. Supplementary Information – Synthetic procedures

The libraries were synthesized through the common approach shown in Scheme 1.[1]



a) De Shong reaction (ref 2); b) H_2/Pd; c) RCO_2H coupling; d) MeONa

SI-Scheme 1. General approach for the synthesis of the ligands

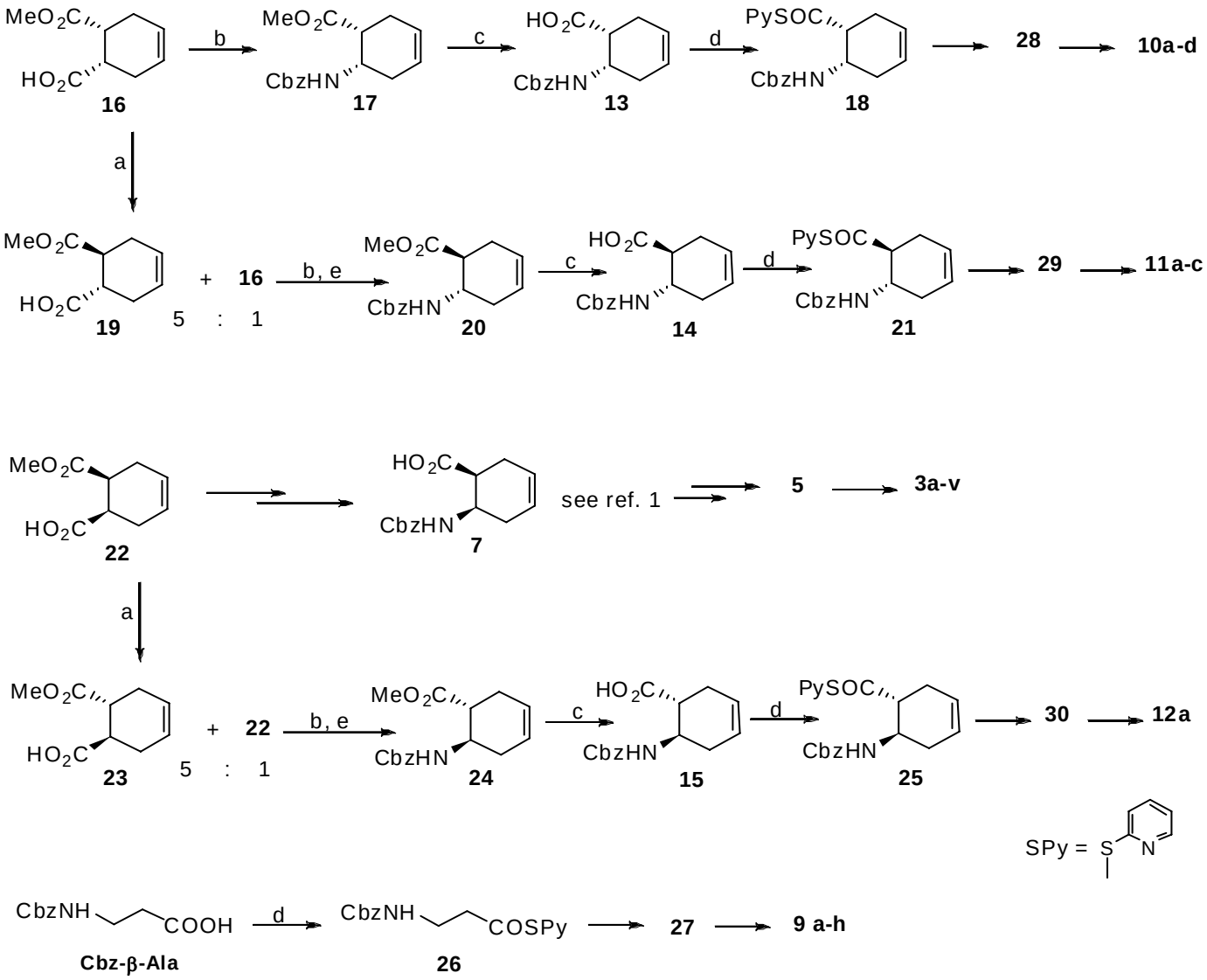
DeShong reaction[2] of tri-*O*-acetyl-fucosylazide **6** with the appropriate *N*-Cbz-protected β-aminoacid (**7**, **13-15**, and *N*-Cbz-Ala) yielded α-*N*-fucosylamides. After Cbz removal, the free amines were coupled with the acid partners (RCO_2H) without previous purification. The synthesis of **3a**,[1] (through intermediates **7** and **5**) and **9a**[3] (through **27**) have been reported elsewhere**.**

Synthesis and activation of the β-aminoacids.

Carbobenzyloxy-β-alanine is commercially available. The synthesis of (1*S*,2*R*)- *N*-Carbobenzyloxy-2-amino-cyclohexanecarboxylic acid **7** has been described.[1] The synthesis of the isomeric *N*-carbobenzyloxy-2-amino-cyclohexanecarboxylic acids **13-15** was performed as shown in Scheme 2, starting from the *cis* monoacids **16** and **22.**[4] They were either transformed directly into the *cis* *N*-Cbz-protected β-aminoacids **13** and **7**, respectively, using a Curtius rearrangement followed by LiOH hydrolysis, or were transformed in the *trans* isomers **19** and **23** by base-promoted equilibration[4b] (Scheme

Supplementary Information

2). Curtius rearrangement of the *trans* monoacids **19** and **23** afforded the corresponding *trans* *N*-Cbz-protected β-aminoacids **14** and **15** after LiOH hydrolysis of esters **20** and **24.**

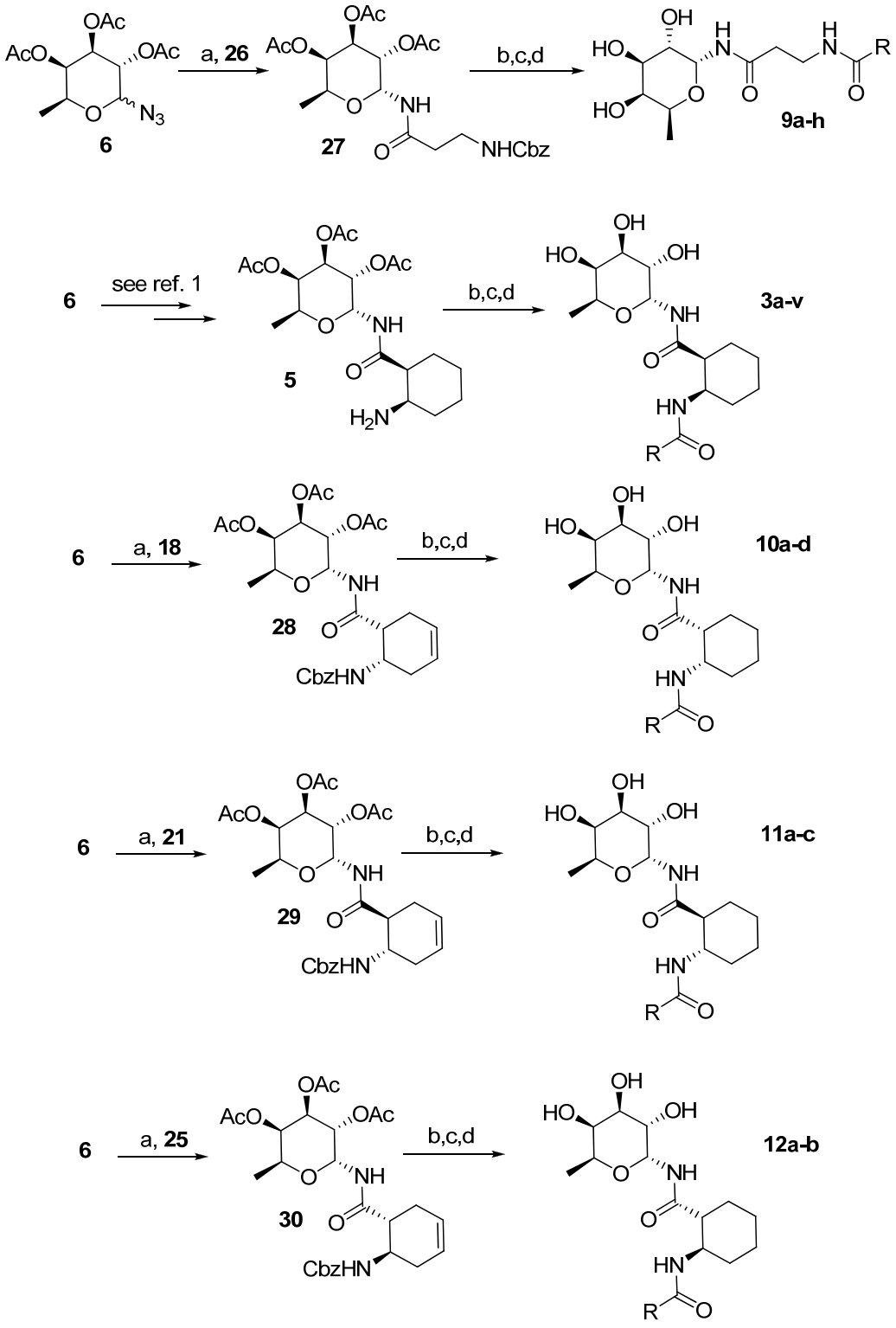


a) tAmOK, THF; b) Curtius rearrangement; c) LiOH; d) Ph_3P, PySSPy; e) flash chromatography

SI-Scheme 2. Synthesis of the β-aminoacids **7, 13-15** and activation as pyridyl thiolesters

All Cbz-protected aminoacids, including commercially available Cbz-β-Ala, were activated as pyridyl thiolesters (**18, 21, 25** and **26**, Scheme 2 and 3) and used in the DeShong reactions with **6** (Scheme 3). The pyridyl thiolesters of Cbz-β-Ala **26** is a known compound.[5]

Supplementary Information



a) Ph_3P, then pyridyl thiolester; b) H_2/Pd; c) RCO_2H, coupling; d) MeONa, MeOH

SI-Scheme 3. DeShong reactions and synthesis of the libraries

This step produced the fucosylamides **5**,[1] **27**,[3] and **28-30**, which were transformed in the final ligands after Cbz removal (H_2/Pd) and coupling with the acid partner.

Supplementary Information

Experimental

Solvents were dried by standard procedures: dichloromethane, methanol, *N*,*N*-diisopropylethylamine and triethylamine were dried over calcium hydride, chloroform and pyridine were dried over activated molecular sieves. Reactions requiring anhydrous conditions were performed under nitrogen. ^{1}H, ^{13}C and ^{31}P-NMR spectra were recorded at 400 MHz on a Bruker AVANCE-400 instrument. Chemical shifts (δ) for ^{1}H and ^{13}C spectra are expressed in ppm relative to internal Me_4Si as standard. Signals were abbreviated as s, singlet; bs, broad singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Mass spectra were obtained with a Bruker ion-trap Esquire 3000 apparatus (ESI ionization) or an Autospec Fission Instrument (FAB ionization). Thin layer chromatography (TLC) was carried out with pre-coated Merck F_{254} silica gel plates. Flash chromatography (FC) was carried out with Macherey-Nagel silica gel 60 (230-400 mesh). The *cis* monoacids **16** and **22** are known and were synthesised as described in the literature.[4] The synthesis of **3a** from **22** through **5** and **7** has already been reported.[1] The pyridyl thiolesters of Cbz-β-Ala **26**[5] and the corresponding fucosylamide **27**,[3] are known compounds.

Synthesis of the *trans* monoacids 19 and 23

29 mL of Potassium *tert*-Amylate (1.7M in Toluene) were diluted in 40 mL of toluene under N_2. The solution was cooled to –15 °C. Then a solution of the *cis* monoacid **16** (or **22**) (3.5 g, 19 mmol) in toluene (20 mL) was added dropwise. The reaction mixture was stirred for 4 hours at - 15 °C. The reaction was quenched with 60 mL HCl (1M), diluted with ethyl acetate and washed with water. The organic phase was dried over Na_2SO_4 and the solvent was evaporated to afford a mixture of product **19** and **16** (or **23** and **22**) as a colourless oil.

Yield (**16**/**19** mixture): 3.3 g (94 %) in a 1:5 ratio.

Yield (**22**/**23** mixture): 2.9 g (84 %) in a 1:4 ratio.

The mixtures **16**/**19** (or **23**/**22**) were used in the general procedure for the *Curtius* rearrangement and the isomers were separated at that level.

Supplementary Information

General procedure for the *Curtius* rearrangement – Synthesis of 17, 20 and 24

DPPA (1.0 mol equivalent) and Et_3N (1 mol equivalent) were added to a 0.3 M solution of the acid in toluene. After the addition of benzyl alcohol (1.8 mol equivalent) the reaction mixture was refluxed for 5 h, then it was diluted with ethyl acetate and extracted with HCl (5 %), saturated $NaHCO_3$ solution and brine. The solvent was evaporated and the *N*-Cbz-protected β-aminoacids were purified by flash-chromatography or automated chromatography on silica gel to give a white solid.

17. Obtained from Curtius rearrangement of **16**[4] and purified by flash chromatography (toluene/ethyl acetate 15:1), R_f = 0.31; Yield (**17**): 4.7 g (75 %)

^{1}H-NMR (400 MHz, $CDCl_3$): 2.14 – 2.22 (m, 1H, H3), 2.28 –2.41 (m, 2H, H3 and H6), 2.46 – 2.54 (m, 1H, H6), 2.79 – 2.83 (m, 1H, H1), 3.67 (s, 3H, COO*Me*), 4.21 – 4.27 (m, 1H, H2), 5.05 – 5.08 (m, 2H, *CH_2*Ph), 5.38 (brd, 1H, NH), 5.56-5.67 (m, 2H, H4 and H5), 7.28 – 7.36 (m, 5H, *Ar*). **^{13}C-NMR (100 MHz, $CDCl_3$):** 25.7 (C6), 30.8 (C3), 42.3 (C1), 47.0 (C2), 52.1 (COO*Me*), 66.9 (*CH_2*Ph), 124.9 (C4 or C5), 125.2 (CH, C4 or C5), 128.3 (CH, Ar), 128.7 (CH, Ar), 136.7 (Cquart., Ar). ESI-MS *m/z* = 312 [$(M + Na)^+$, 100 %].

20. Obtained from Curtius rearrangement of a 5:1 **19:16** mixture and separated from the *cis* isomer by automated chromatography (toluene/ethyl acetate with a gradient from 0 % to 10 % ethyl acetate), R_f = 0.31 (toluene/EtOAc 19:1). Yield (**20**): 1.7 g (38 %)

^{1}H-NMR (400 MHz, $CDCl_3$): 1.92 –2.00 (m, 1H, H3), 2.24 – 2.31 (m, 1H, H6), 2.45 – 2.52 (m, 2H, H3 and H6), 2.67 – 2.73 (m, 1H, H1), 3.63 (s, 3H, COO*Me*), 4.04 – 4.12 (m, 1H, H2), 4.86 (brs, 1H, NH), 5.08 (s, 2H, *CH_2*Ph), 5.56 – 5.59 (m, 1H, H4), 5.62 – 5.66 (m, 1H, H5), 7.27 – 7.35 (m, 5H, *Ar*). **^{13}C-NMR (100 MHz, $CDCl_3$)**: 26.8 (C6), 31.3 (C3), 44.6 (C1), 48.1 (C2), 52.1 (COO*Me*), 66.9 (*CH_2*Ph), 124.3 (C4), 125.2 (C5), 128.3 (Ar), 128.7 (Ar), 128.7 (Ar), 136.7 (Cquart., Ar), 155.7 (NHCO), 174.1 (COOMe). ESI-MS *m/z* = 312 [$(M + Na)^+$, 100 %]

24. Obtained from Curtius rearrangement of a 5:1 **23:22** mixture and separated from the *cis* isomer by automated chromatography (toluene/ethyl acetate with a gradient from 0 % to 10 % ethyl acetate), R_f = 0.31 (toluene/EtOAc 19:1); Yield (**24**): 1.1 g (32 %).

Supplementary Information

^{1}H-NMR (400 MHz, $CDCl_3$): 1.92 – 2.00 (m, 1H, H3), 2.24 – 2.32 (m, 1H, H6), 2.46 – 2.51 (m, 2H, H3 and H6), 2.67 – 2.73 (m, 1H, H1), 3.62 (s, 3H, COO*Me*), 4.06 – 4.13 (m, 1H, H2), 4.84 (brs, 1H, NH), 5.08 (s, 2H, CH_2Ph), 5.56 – 5.59 (m, 1H, H4), 5.63 – 5.66 (m, 1H, H5), 7.26 – 7.36 (m, 5H, Ar). **^{13}C-NMR (100 MHz, $CDCl_3$)**: 26.8 (C6), 31.2 (C3), 44.6 (C1), 48.1 (C2), 52.2 (COO*Me*), 66.9 (CH_2Ph), 124.3 (C4), 125.2 (C5), 128.4 (Ar), 128.7 (Ar), 128.8 (Ar), 136.6 (Cquart., Ar), 174.1 (COOMe). ESI-MS *m/z* = 312 [$(M + Na)^+$, 100 %]

Ester hydrolysis – Synthesis of *N*-Cbz-β-aminoacids 13 - 15

A 0.17 M solution of β-amino ester **17** (or **20** or **24**) in MeOH/H_2O (4:1) was prepared. LiOH*H_2O (2.4 mol equivalents) was added to the solution at 0 °C and the mixture was stirred for 12 h at room temperature. After the reaction was completed, ca. 2/3 of the solvent was evaporated and, if necessary, the pH of the mixture was adjusted to pH 9 with $NaHCO_3$. To remove benzyl alcohol that was occasionally still present after the previous reaction step, the mixture was extracted with diethyl ether. Then the inorganic phase was acidified to pH 1 with HCl (6M) and extracted with ethyl acetate. The organic phases were combined and the solvent was evaporated to afford the acid (**13** or **14** or **15**) as a white solid.

13 Yield (**13**): 4.29 g (93 %)

^{1}H-NMR (400 MHz, $CDCl_3$): 2.16 – 2.23 (m, 1H, H3), 2.34 – 2.39 (m, 2H, H3 and H6), 2.48 – 2.55 (m, 1H, H6), 2.85 – 2.90 (m, 1H, H1), 4.17 – 4.28 (m, 1H, H2), 5.03 – 5.11 (m, 2H, CH_2Ph), 5.46 (brd, 1H, NH), 5.59 - 5.67 (m, 2H, H4 and H5), 7.27 – 7.35 (m, 5H, Ar). **^{13}C-NMR (100 MHz, $CDCl_3$)**: 26.1 (C6), 30.6 (C3), 42.1 (C1), 46.9 (C2), 67.1 (CH_2Ph), 125.0 (C4 or C5), 125.1 (C4 or C5), 128.4 (CH, Ar), 128.8 (CH, Ar), 178.6 (COOH). ESI-MS *m/z* = 298 [$(M + Na)^+$, 59 %].

14 Yield (**14**): 0.64 g (83 %)

^{1}H-NMR (400 MHz, $CDCl_3$): 1.96 - 2.05 (m, 1H, H3), 2.31 – 2.40 (m, 1H, H6), 2.46 – 2.56 (m, 2H, H3 and H6), 2.76 – 2.81 (m, 1H, H1), 4.10 – 4.15 (m, 1H, H2), 4.97 (brd, 1H, NH), 5.04 – 5.14 (m, 2H, CH_2Ph), 5.59 – 5.69 (m, 2H, H4 and H5), 7.29 – 7.38 (m, 5H, Ar). **^{13}C-NMR (100 MHz, $CDCl_3$)**: 26.4 (C6), 30.9

(C3), 43.9 (C1), 47.7 (C2), 67.0 (*CH*$_2$Ph), 124.4 (C4 or C5), 125.1 (C4 or *C5*), 128.38 (Ar), 128.75 (Ar), 136.5 (Cquart., Ar), 163.5 (NHCO), 178.5 (COOH). ESI-MS *m/z* = 298 [(M + Na)$^+$, 11 %]

15 Yield (**15**): 643 mg (43%)

^{1}H-NMR (400 MHz, CDCl$_3$): 1.93 – 2.03 (m, 1H, H3), 2.28 – 2.41 (m, 1H, H6), 2.42 – 2.57 (m, 2H, H3 and H6), 2.73 – 2.81 (m, 1H, H1), 4.06 – 4.16 (m, 1H, H2), 4.92 (brd, 1H, NH), 5.03 – 5.13 (m, 2H, *CH*$_2$Ph), 5.55 – 5.60 (m, 1H, H4), 5.62 – 5.67 (m, 1H, H5), 7.28 – 7.38 (m, 5H, Ar). **^{13}C-NMR (100 MHz, CDCl$_3$)**: 26.3 (C6), 30.7 (C3), 43.7 (C1), 47.5 (C2), 66.9 (*CH*$_2$Ph), 124.2 (C4 or C5), 124.9 (C4 or *C5*), 128.2 (Ar), 128.56 (Ar), 128.6 (Ar). ESI-MS *m/z* = 298 [(M + Na)$^+$, 11 %]

Synthesis of pyridyl thiolesters 18, 21, 25

PPh_3 (1.3 mol equivalent) and dipyridyl disulfide (1.3 mol equivalent) were added to a 0.1 M solution of **13** (or **14** or **15**) in CH_3CN. The reaction mixture was refluxed for 2 h, then the solvent was evaporated and the product (**18** or **21** or **25**) was isolate by flash chromatography on a short path of SiO_2 (*n*-hexane/ethyl acetate 6:4 or 7:3).

18 Yield (**18**): 830 mg (79 %), R_f = 0.25 (n-hexane/ethyl acetate 7:3)

^{1}H-NMR (400 MHz, CDCl$_3$): 2.21 – 2.38 (m, 1H, H3), 2.38 – 2.48 (m, 2H, H3 and H6), 2.56 – 2.65 (m, 1H, H6), 3.17 – 3.21 (m, 1H, H1), 4.33 – 4.39 (m, 1H, H2), 5.07 (s, 2H, *CH*$_2$Ph), 5.26 (brd, 1H, NH), 5.61-5.72 (m, 2H, H4 and H5), 7.25 – 7.34 (m, 6H, Ar and Pyr), 7.55 – 7.58 (m, 1H, Pyr), 7.67 – 7.71 (m, 1H, Pyr), 8.58 – 8.61 (m, 1H, Pyr)

21 Yield (**21**): 528 mg (79 %), R_f = 0.25 (n-hexane/ethyl acetate 7:3)

^{1}H-NMR (100 MHz, CDCl$_3$): 2.04 – 2.13 (m, 1H, H6), 2.38 – 2.54 (m, 3H, H3 and H6), 3.06 – 3.14 (m, 1H, H1), 4.12 – 4.19 (m, 1H, H2), 4.99 (brd, 1H, NH), 5.09 (s, 2H, *CH*$_2$Ph), 5.58 - 5.69 (m, 2H, H4 and H5), 7.26 – 7.35 (m, 6H, Ar and pyr), 7.51 - .53 (m, 1H, pyr), 7.66 – 7.70 (m, 1H, pyr), 8.57 – 8.60 (m, 1H, pyr).

Supplementary Information

25 Yield (**25**): 334 mg (83 %), R_f = 0.33 (n-hexane/ethyl acetate 6:4)

^{1}H-NMR (400 MHz, $CDCl_3$): 2.03 – 2.14 (m, 1H, H6), 2.39 – 2.54 (m, 3H, H3 and H6), 3.07 – 3.14 (m, 1H, H1), 4.12 – 4.19 (m, 1H, H2), 4.96 – 5.03 (brd, 1H, NH), 5.08 (s, 2H, *CH_2*Ph), 5.58 – 5.69 (m, 2H, H4 and H5), 7.24 – 7.34 (m, 6H, Ar and pyr), 7.51 – 7.53 (m, 1H, pyr), 7.66 – 7.71 (m, 1H, pyr), 8.58 – 8.61 (m, 1H, pyr).

DeShong reaction. Synthesis of the α-fucosylamides 28-30

To a 0.07 M solution of fucosyl azide **6** in $EtNO_2$ grounded molecular sieves and a 0.08 M solution of PPh_3 (1.1 mol equivalent) in $EtNO_2$ were added. The reaction mixture was refluxed for 14 h. After cooling to room temperature, a 0.5 M solution of pyridyl thiolester **18** (or **21** or **25**) (1.3 mol equivalent) in $EtNO_2$ and $CuCl_2$*H_2O(1.3 mol equivalent) were added to the reaction mixture. The mixture was stirred at 40 °C for 24 h monitoring by TLC. After completion, molecular sieves and catalyst were filtered on a celite pad washing with ethyl acetate, the organic phase was extracted with NH_3/NH_4Cl (1:1) and washed with water. The organic phase was dried over Na_2SO_4 and the solvent was evaporated. The obtained crude was purified by flash-chromatography on SiO_2 (*n*-hexane/ethyl acetate 6:4).

28 Yield (**28**): 320 mg (31 %), R_f = 0.22 (*n*-hexane/ethyl acetate 6:4)

^{1}H-NMR (400 MHz, $CDCl_3$): 1.15 (d, $J_{5\text{-}6}$ = 6.4 Hz, H_{F6}), 1.94 (s, 3H, Fuc-Ac), 1.96 (s, 3H, Fuc-Ac), 2.05 – 2.14 (m, 1H, H_{Cy3ax}), 2.15 (s, 3H, Fuc-*Ac*), 2.19 – 2.25 (m, 1H, H_{Cy6ax}), 2.43 – 2.51 (m, 1H, H_{Cy3eq}), 2.54 – 2.63 (m, 1H, H_{Cy6eq}), 2.70 – 2.75 (m, 1H, H_{Cy1}), 4.02 – 4.08 (m, 1H, H_{F5}), 4.32 – 4.38 (m, 1H, H_{Cy2}), 5.06 (d, *J* = 12.2 Hz, 1H, *CH_2*Ph), 5.16 (d, *J* = 12.2 Hz, 1H, *CH_2*Ph), 5.29 - 5.36 (m, 4H, H_{F4}, H_{F3}, Cy-*NH*, H_{F2}), 5.62 – 5.80 (m, 2H, H_{Cy4} and H_{Cy5}), 5.94 (dd, *J* = 4.3 Hz, *J* = 8.1 Hz, 1H, H_{F1}), 7.28 – 7.36 (m, 5H, Ar), 7.55 (brs, 1H, Fuc-*NH*). **^{13}C-NMR (100 MHz, $CDCl_3$)**: 16.5 (C_{F6}), 20.8 (Fuc-Ac-Me), 20.9 (Fuc-Ac-Me), 25.6 (C_{Cy6}), 32.4 (C_{Cy3}), 44.1 (C_{Cy1}), 46.2 (C_{Cy2}), 66.3 (H_{F5}), 66.4 (C_{F2}), 67.6 (CH_2, *CH_2*Ph), 68.3 (C_{F3}), 70.9 (C_{F4}), 74.6 (C_{F1}), 124.4 (C_{Cy4} or C_{Cy5}), 126.4 (C_{Cy4} or C_{Cy5}), 128.4 (Ar), 128.5 (Ar), 128.8 (Ar), 136.3 (Cquart., Ar),

157.4 (Cquart.), 169.7 (Cquart.), 170.2 (Cquart), 170.9 (Cquart.), 173.4 (Cquart.). ESI-MS m/z = 569 [(M + Na)$^+$, 100 %]. $[\alpha]_D$ = -17.8 (c = 1.50, EtOH)

29 Yield (**29**): 210 mg (46 %), R_f = 0.15 (*n*-hexane/ethyl acetate 6:4)

^{1}H-NMR (400 MHz, $CDCl_3$): 1.02 (d, 3H, $J_{5\text{-}6}$ = 6.3 Hz, H_{F6}), 1.98 (s, 6H, Fuc-Ac), 2.12 (s, 3H, Fuc-Ac), 2.14 – 2.20 (m, 1H, H_{Cy3ax}), 2.21 – 2.45 (m, 1H, H_{Cy6ax}, H_{Cy3eq}, H_{Cy6eq}), 2.83 – 2.89 (m, 1H, H_{Cy1}), 3.82 – 3.89 (m, 1H, H_{Cy2}), 3.89 – 3.98 (m, 1H, H_{F5}), 5.00 – 5.09 (m, 2H, *CH*$_2$Ph), 5.19 – 5.22 (m, 1H, H_{F4}), 5.27 – 5.35 (m, 1H, Cy-*NH*, H_{F3}, H_{F2}), 5.55 – 5.60 (m, 1H, H_{Cy4}), 5.63 – 5.68 (m, 1H, H_{Cy5}), 5.91 (dd, *J* = 4.6 Hz, *J* = 8.1 Hz 1H, H_{F1}) 7.26 – 7.34 (m, 5H, Ar), 7.42 (brs, 1H, Fuc-*NH*). **^{13}C-NMR (100 MHz, $CDCl_3$)**: 16.3 (C_{F6}), 20.8 (Fuc-Ac-*Me*), 20.9 (Fuc-Ac-*Me*), 21.0 (Fuc-Ac-*Me*), 28.7 (C_{Cy6}), 31.3 (C_{Cy3}), 46.3 (C_{Cy1}), 49.1 (C_{Cy2}), 65.8 (C_{F5}), 66.3 (C_{F2}), 67.2 (*CH*$_2$Ph), 68.4 (C_{F3}), 70.9 (C_{F4}), 74.6 (C_{F1}), 124.6 (C_{Cy4}), 125.6 (C_{Cy5}), 128.2 (Ar), 128.5 (Ar), 128.8 (Ar), 136.3 (Cquart, Ar), 156.6 (Cquart.), 169.7 (Cquart.), 170.6 (Cquart.), 171.0 (Cquart.), 174,7 (Cquart.) ESI-MS m/z = 569 [(M + Na)$^+$, 100 %]. $[\alpha]_D$ = -93.7 (c = 0.50, MeOH)

30 Yield (**30**): 200 mg (52%), R_f = 0.15 (*n*-hexane/ethyl acetate 6:4)

^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.04 (d, 3H, J_{5-6} = 6.4 Hz, H_{F6}), 1.96 (s, 3H, OAc), 1.98 (s, 3H, OAc), 2.05 – 2.12 (m, 1H, H_{C3ax}), 2.15 (s, 3H, OAc), 2.24 – 2.48 (m, 3H, H_{C3eq} and H_{C6}), 2.74 – 2.87 (m, 1H, H_{Cy1}), 3.88 – 3.99 (m, 2H, H_{Cy2} and H_{F5}), 5.03 – 5.12 (m, 3H, *CH*$_2$Ph and Cyc-*NH*), 5.23 – 5.25 (m, 1H, H_{F2}), 5.32 – 5.38 (m, 2H, H_{F3} and H_{F4}), 5.57 –5.62 (m, 1H, H_{Cy4} or H_{Cy5}), 5.64 – 5-70 (m, 1H, H_{Cy4} or H_{Cy5}), 5.85 – 5.91 (m, 1H, H_{F1}), 7.27 – 7.36 (m, 6H, Ar and Fuc-NH). **^{13}C-NMR (100 MHz, $CDCl_3$):** δ (ppm) = 16.3 (C_{F6}), 20.8 (Fuc-OAc-Me), 20.9 (Fuc-OAc-Me), 20.9 (Fuc-OAc-Me), 29.5 (C_{Cy6}), 32.0 (C_{Cy3}), 47.4 (C_{Cy1}), 48.7 (C_{Cy2}), 66.02 (C_{F5}), 66.4 (C_{F3} or C_{F4}), 67.4 (*CH*$_2$-Ph), 68.3 (C_{F3} or C_{F4}), 70.9 (C_{F2}), 74.8 (C_{F1}), 124.4 (C_{Cy4} or C_{Cy5}), 125.8 (C_{Cy4} or C_{Cy5}), 128.3 (Ar), 128.6 (Ar), 128.9 (Ar), 136.1 (Cquart., Ar), 156.8 (Cquart.), 169.7 (Cquart.), 170.4 (Cquart.), 170.9 (Cquart.), 174.4 (Cquart.). ESI-MS *m/z* = 569 [(M + Na)$^+$, 100 %].

Supplementary Information

Synthesis of the ligands 3, 9-12

The fucosylamides isolated after the DeShong reaction were treated with H_2 and Pd/C in MeOH (0.05 M) for 2h at room temperature. The crude was filtered through celite and used for the coupling reactions, which were run using the general procedures for coupling reported below for amine **5.** The final amides were deacetylated using the general procedure for Zemplen's deprotection described below for compound **8**.

General procedure of acetylation with Ac_2O

To a solution of **5** (0.072 mmol, 1 equiv) in CH_2Cl_2 (2 mL), pyridine (0.01 mL, 1.3 equiv) and Ac2O (0.01 mL, 1.3 equiv) were added and the solution was stirred overnight. The mixture was diluted with CH_2Cl_2, extracted with water, diluted HCl, water. The organic phase was dried over Na_2SO_4 and evaporated.

General procedure of coupling using HBTU

To a solution of **5** (0.02 mmol) in 0.2 mL of CH_2Cl_2, Et_3N (0.072 mmol, 3 eq.) and carboxylic partner (0.036 mmol, 1.5 eq.) in 0.2 mL of CH_2Cl_2 were added. Subsequently, HBTU (0.036 mmol, 1.5 eq.) was added and reaction mixture stirred at room temperature. After 18 h, 10 mL of CH_2Cl_2 were added to the reaction mixture and organic phase was washed with 0.5 M NaOH (10 mL), 1M $KHSO_4$ (10 mL), water (10 mL) and brine (10 mL). The organic phase was dried over Na_2SO_4, filtered and the solvent evaporated under vacuum. The residue was purified via Biotage using the appropriate solvent gradient.

General procedure of coupling using acid chloride

The carboxylic partner (1.2 mmol, 1.2 eq.) was refluxed in 1 mL of toluene in presence of oxalyl chloride (3 mmol, 3.3 eq.) during 3 h. The solution was then evaporated and added to a solution of **5** (1 mmol) and Et_3N (2 mmol, 2 eq.) in 1 mL of THF. The solution was stirred at room temperature for 18 h. After completion, the solvent was evaporated. The crude was taken up with CH_2Cl_2, was washed with a saturated solution of $NaHCO_3$, 10% citric acid, and an aqueous saturated NaCl solution. Separations have been done using isolute column separative phase. The solvent was evaporated under vacuum and the residue was purified via Biotage using the appropriate solvent gradient.

Supplementary Information

General procedure of coupling using EDC/HOBt

To the mixture of the acidic partner (0.07 mmol, 1.1 eq.) in 1.5 mL of CH_2Cl_2 were added HOBt (0.10 mmol, 1.4 eq.) and compound **5** (0.07 mmol, 1 eq.). The mixture was stirred at 0°C for 5 min then a solution of EDC.HCl (0.09 mmol, 1.3 eq.) and triethylamine (0.09 mmol, 1.2 eq.) in 0.5 mL of CH_2Cl_2 was added. The resulting mixture was allowed to warm at r.t and stirred at r.t overnight. The reaction was then washed with $NaHCO_3$, 10% citric acid, and an aqueous saturated NaCl solution. Separations were performed using isolute column separative phase. The solvent was evaporated under vacuum and the residue was purified via Biotage using the appropriate solvent gradient.

General procedure of Zemplen's deprotection

To a solution of protected amide **8** (0.07 mmol) in 1.5 mL of dry MeOH, NaOMe (0.01 mmol) was added and the solution was stirred at room temperature. After completion, amberlite IRA 120^+ was added until pH 7 and the beads were filtered off. The solvent was evaporated under vacuum and the residue was purified by reverse phase automated chromatography using the appropriate solvent gradient.

(1*S*,2*R*)-2-Aminocyclohexanecarboxylic acid series: Ligands 3

***N*-[(1*S*,2*R*)-2-(3-Hydroxybenzamido)cyclohexanecarboxyl]-α-L-fucopyranosylamine (3b)**

Compound **5**[13] was coupled with 3-acetoxybenzoic acid using the general HBTU procedure. The crude was purified by flash chromatography (1:4 hexane:AcOEt , R_f = 0.63, 72% yield). Zemplen deprotection and flash chromatography (85:15 $CHCl_3$:MeOH, R_f = 0.21) afforded **3b** (quant). **^{1}H-NMR (400 MHz, CD_3OD):** δ (ppm) = 0.88 (d, 3H, $J_{5\text{-}6}$ = 6.4 Hz, H_{F6}), 1.31-2.17 (m, 8H, CH_{2Cy}), 2.94 (m, 1H, H_{Cy1}), 3.54 (m, 1H, H_{F4}), 3.59 (m, 1H, H_{F5}), 3.75 (dd, 1H, $J_{2\text{-}3}$ = 10.3 Hz, $J_{3\text{-}4}$ = 3.3 Hz, H_{F3}), 3.93 (dd, 1H, $J_{1\text{-}2}$ = 5.6 Hz, H_{2F}), 4.37 (m, 1H, H_{Cy2}), 5.50 (d, 1H, H_{F1}), 6.94 (m, 1H, H_{Ar}), 7.19-7.27 (m, 3H, H_{Ar}); **^{13}C-NMR (100 MHz, CD_3OD) :** δ (ppm) = 16.8 (C_{F6}), 23.3, 23.5, 26.2, 30.7 (4×CH_{2Cy}), 46.0 (C_{Cy1}), 50.3 (C_{Cy2}), 68.0 (C_{F2}), 68.4 (C_{F5}), 71.5 (C_{F3}), 73.4 (C_{F4}), 78.5 (C_{F1}), 115.4 (CH_{Ar}), 119.4 (CH_{Ar}), 119.8 (CH_{Ar}), 130.8 (CH_{Ar}), 137.4 (C_{Ar}), 159.0 (C_{Ar}), 170.2 (C=O), 177.8 (C=O). R_f = 0.21 (4:1 $CHCl_3$:MeOH). ESI-MS: *m/z*

= 391 [(M-OH)$^+$, 100%]. HR-MS (ESI): calculated for $C_{20}H_{28}N_2O_7$ [M+Na]$^+$: 431.17887; found [M+Na]$^+$: 486.17851.

***N*-[(1*S*,2*R*)-2-(3,5-Dihydroxybenzamido)cyclohexanecarboxyl]-α-L-fucopyranosylamine (3c)**

Compound **5**[13] was coupled with 3,5-diacetoxybenzoic acid using the general HBTU procedure. The crude was purified by flash chromatography (1:1.5 hexane-AcOEt, R_f =0.33, 55 % yield) Zemplen deprotection and flash chromatography (85:15 $CHCl_3$: MeOH, R_f = 0.18) afforded **3c** (quant). **^{1}H-NMR (400 MHz, CD_3OD) :** δ (ppm) = 0.89 (d, 1H, $J_{5\text{-}6}$ = 6.4 Hz, H_{F6}), 1.78-1.29 (m, 6H, H_{Cy3}, $2H_{Cy4}$, $2H_{Cy5}$, H_{Cy6}), 1.96-1.85 (m, 1H, H_{Cy6}), 2.16-2.07 (m, 1H, H_{Cy3}), 2.89 (td, 1H, J = 8.4 & 4.2 Hz, H_{Cy1}), 3.53 (d, 1H, $J_{3\text{-}4}$ = 3.2 Hz, H_{F4}), 3.57 (q, 1H, $J_{5\text{-}6}$ = 6.6 Hz, H_{F5}), 3.73 (dd, 1H, $J_{2\text{-}3}$ = 10.3 Hz, $J_{3\text{-}4}$ = 3.4 Hz, H_{F3}), 3.91 (dd, 1H, $J_{2\text{-}3}$ = 10.3 Hz, $J_{1\text{-}2}$ = 5.6 Hz, H_{F2}), 4.32-4.25 (m, 1H, H_{Cy2}), 5.45 (d, 1H, $J_{1\text{-}2}$ = 5.6 Hz, H_{F1}), 6.37 (t, 1H, J = 2.2 Hz, CH_{Ar}), 6.64 (d, 2H, J = 2.2 Hz, $2CH_{Ar}$); **^{13}C-NMR (100 MHz, CD_3OD) :** δ (ppm) = 16.7 (C_{F6}), 23.2 (C_{Cy4}), 24.3 (C_{Cy5}), 26.1 (C_{Cy6}), 30.6 (C_{Cy3}), 45.8 (C_{Cy1}), 50.2 (C_{Cy2}), 67.9 (C_{F2}), 68.4 (C_{F5}), 71.4 (C_{F3}), 73.3 (C_{F4}), 78.4 (C_{F1}), 106.7 (CH_{Ar}), 106.8 (CH_{Ar}), 127.7 (CH_{ArTrp}), 138.0 (C_{Ar}), 160.0 ($2xC_{Ar}$), 170.2 (C=O), 177.7 (C=O). R_f = 0.17 (4:1 $CHCl_3$:MeOH). ESI-MS: *m/z* = 447.4 [(M+Na)$^+$, 100%]. HR-MS (ESI): calculated for $C_{20}H_{28}N_2O_8$ [M+Na]$^+$: 447.17397; found [M+Na]$^+$: 486.17400.

***N*-[(1*S*,2*R*)-2-(3-Pyridinecarboxamido)cyclohexanecarboxyl]-α-L-fucopyranosylamine (3d)**

Compound **5**[13] was coupled with nicotinic acid using the general HBTU procedure. The crude was purified by flash chromatography (AcOEt, R_f = 0.30, 77% yield). Zemplen deprotection and flash chromatography (8:2 $CHCl_3$:MeOH, R_f = 0.33) afforded **3d** (95% yield). **^{1}H-NMR (400 MHz, D_2O) :** δ (ppm) = 0.70 (3H, d, $J_{5\text{-}6}$ = 6.5 Hz, H_{F6}), 1.35-1.91 (m, 8H, CH_{2Cy}), 2.91 (m, 1H, H_{Cy1}), 3.55 (m, 1H, H_{F5}), 3.36 (pseudo-d,1H, $J_{4\text{-}5}$ = 3.4 Hz, H_{F4}), 3.77 (dd, 1H, $J_{2\text{-}3}$ = 10.6 Hz, H_{F3}), 3.92 (dd, 1H, $J_{1\text{-}2}$ = 5.7 Hz, H_{F2}), 4.47 (m, 1H, H_{Cy2}), 5.43 (d, 1H, H_{F1}), 7.52 (dd, 1H, J = 5.0 Hz, J = 7.7 Hz, H_{Ar}), 8.05 (d, 1H, J = 8.0 Hz, H_{Ar}), 8.69 (m, 2H, H_{Ar}). **^{13}C-NMR (100 MHz, D_2O) :** δ (ppm) = 16.2 (C_{F6}), 20.6, 23.6, 30.3 ($4xCH_{2Cy}$), 45.6 (C_{Cy1}), 49.7 (C_{Cy2}), 66.7 (C_{F2}), 67.9 (C_{F5}), 70.3 (C_{F3}), 72.1 (C_{F4}), 77.5 (C_{F1}), 137.1, 148.2,

152.4 (4xC_{Ar}), 169.1 (C=O), 178.6 (C=O). R_f = 0.33 ($CHCl_3$/MeOH = 4/1). ESI-MS: *m/z* = 394.4 [$(M+H)^+$, 43%]. HR-MS (ESI): calculated for $C_{19}H_{27}N_3O_6$ $[M+Na]^+$: 416.17921; found $[M+Na]^+$: 416.17906.

***N*-[(1*S*,2*R*)-2-(3-Methoxybenzamido)cyclohexanecarboxyl]-α-L-fucopyranosylamine (3e)**

Compound **5**[13] was coupled with 3-methoxybenzoic acid using the general HBTU procedure. The crude was purified by flash chromatography (1:1.5 hexane-AcOEt, R_f =0.31, 64 % yield) Zemplen deprotection and flash chromatography (85:15 $CHCl_3$: MeOH, R_f = 0.30) afforded **3e** (quant). **^{1}H-NMR (400 MHz, CD_3OD) :** δ (ppm) = 0.83 (d, 1H, $J_{5\text{-}6}$ = 6.5 Hz, H_{F6}), 1.79-1.34 (m, 6H, H_{Cy3}, $2H_{Cy4}$, $2H_{Cy5}$, H_{Cy6}), 2.02-1.89 (m, 1H, H_{Cy6}), 2.18-2.10 (m, 1H, H_{Cy3}), 2.92 (td, 1H, *J* = 8.6 & 4.3 Hz, H_{Cy1}), 3.51 (d, 1H, $J_{3\text{-}4}$ = 2.5 Hz, H_{F4}), 3.56 (q, 1H, $J_{5\text{-}6}$ = 6.5 Hz, H_{F5}), 3.73 (dd, 1H, $J_{2\text{-}3}$ = 10.4 Hz, $J_{3\text{-}4}$ = 3.4 Hz, H_{F3}), 3.83 (s, 3H, OMe), 3.91 (dd, 1H, $J_{2\text{-}3}$ = 10.4 Hz, $J_{1\text{-}2}$ = 5.6 Hz, H_{F2}), 4.40-4.33 (m, 1H, H_{Cy2}), 5.46 (d, 1H, $J_{1\text{-}2}$ = 5.6 Hz, H_{F1}), 7.07 (td, 1H, *J* = 6.0 & 2.7 Hz, H_{Ar}), 7.35 (m, 3H, $3H_{Ar}$);**^{13}C-NMR (100 MHz, CD_3OD) :** δ (ppm) = 16.8 (C_{F6}), 23.2 (C_{Cy5}), 24.3 (C_{Cy4}), 26.0 (C_{Cy6}), 30.7 (C_{Cy3}), 45.9 (C_{Cy1}), 50.3 (C_{Cy2}), 55.9 (OMe), 67.9 (C_{F2}), 68.3 (C_{F5}), 71.4 (C_{F3}), 73.3 (C_{F4}), 78.4 (C_{F1}), 113.9 (CH_{Ar}), 118.5 (CH_{Ar}), 120.6 (CH_{Ar}), 130.7 (CH_{Ar}), 137.4 (C_{Ar}), 161.3 (C_{ArOMe}), 169.9 (C=O), 177.7 (C=O). R_f = 0.40 ($CHCl_3$/MeOH = 4/1). ESI-MS: *m/z* = 445.3 [$(M+Na)^+$, 100%]. HR-MS (ESI): calculated for $C_{21}H_{30}N_2O_7$ $[M+Na]^+$: 445.19452; found $[M+Na]^+$: 445.19401.

***N*-[(1*S*,2*R*)-2-((2*R*)-2-Hydroxy-phenylacetamido)cyclohexanecarboxyl]-α-L-fucopyranosylamine (3f)**

Compound **5**[13] was coupled with (*R*)-(−)-α-acetoxyphenylacetic acid using the general acid chloride procedure. The crude was purified by flash chromatography (1:4 hexane:AcOEt, R_f = 0.6, 60% yield). Zemplen deprotection and flash chromatography (8:2 $CHCl_3$: MeOH, R_f = 0.25) afforded **3f** (quant). **^{1}H-NMR (400 MHz, CD_3OD) :** δ (ppm) = 0.96 (d, 3H, $J_{5\text{-}6}$ = 6.4 Hz, H_{F6}), 1.40-2.08 (m, 8H, CH_{2Cy}), 2.76 (m, 1H, H_{Cy1}), 3.57 (m, 1H, H_{F4}), 3.65 (dq, 1H, $J_{4\text{-}5}$ < 1Hz, H_{F5}), 3.73 (dd, 1H, $J_{2\text{-}3}$ = 10.3 Hz, $J_{3\text{-}4}$ = 3.6 Hz, H_{F3}), 3.95 (dd, 1H, $J_{1\text{-}2}$ = 5.6 Hz, H_{F2}), 4.16 (m, 1H, H_{Cy2}), 4.98 (s, 1H, -C*H*(OH)Ph), 5.51 (d, 1H, H_{F1}), 7.26-7.42 (m, 5H, H_{Ar}). **^{13}C-NMR (100 MHz, CD_3OD) :** δ (ppm) = 17.1 (C_{F6}), 23.3, 24.3, 26.7,

30.9 (4xCH_{2Cy}), 46.4 (C_{Cy1}, C_{Cy2}), 68.2 (C_{F2}), 68.5 (C_{F5}), 71.6 (C_{F3}), 73.5 (C_{F4}), 75.7 (-*C*H(OH)Ph), 78.4 (C_{F1}), 128.6 (2xCH_{Ar}), 129.2 (CH_{Ar}), 129.6 (2×CH_{Ar}), 141.8 (C_{Ar}), 174.6, 177.5 (2×C=O). R_f = 0.25 (4:1 $CHCl_3$:MeOH). ESI-MS: *m/z* = 445 [$(M+Na)^+$, 25%]. HR-MS (ESI): calculated for $C_{21}H_{30}N_2O_7$ $[M+Na]^+$: 445.19452; found $[M+Na]^+$: 445.19406.

***N*-[(1*S*,2*R*)-2-(D-*N'*-Acetyl-triptophanoyl)cyclohexanecarboxyl]-α-L-fucopyranosylamine (3g)**

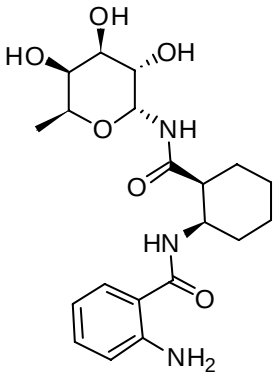
Compound **5**[13] was coupled with D-N-acetyl-triptophane using the general HBTU procedure. The crude was purified by flash chromatography (100:2 $CHCl_3$: MeOH, R_f = 0.28, 85% yield). Zemplen deprotection and flash chromatography (85:15 $CHCl_3$: MeOH, R_f = 0.23) afforded **3g** (quant). **^{1}H-NMR (400 MHz, CD_3OD) :** δ (ppm) = 1.17 (d, 1H, J_{5-6} = 6.5 Hz, H_{F6}), 1.36-1.12(m 4H, CH_{2Cy}), 1.73-1.54 (m, 4H, CH_{2Cy}), 1.95 (s, 3H, CH_3CONH-), 2.70-2.63 (m, 1H, H_{Cy1}), 3.09 (dd, 1H, *J* = 14.4 & 7.4 Hz, CH_{2Trp}), 3.23 (dd, 1H, *J* = 14.4 & 7.2 Hz, CH_{2Trp}), 3.64 (d, 1H, J_{3-4} = 3.0 Hz, H_{4F}), 3.80-3.74 (m, 2H, H_{F3}, H_{F5}), 3.95 (dd, 1H, J_{2-3} = 10.3, J_{1-2} = 5.6 Hz, H_{F2}), 4.16-4.10 (m, 1H, H_{Cy2}), 4.66 (t, 1H, *J* = 7.3 Hz, CH_{Trp}), 5.48 (d, 1H, J_{1-2} = 5.6 Hz, H_{F1}), 7.02 (t, 1H, *J* = 7.0 Hz, CH_{ArTrp}), 7.12-7.06 (m, 2H, 2CH_{ArTrp}), 7.33 (d, 2H, *J* = 8.1 Hz, CH_{ArTrp}), 7.60 (d, 1H, *J* = 7.8 Hz, CH_{ArTrp}); **^{13}C-NMR (100 MHz, CD_3OD) :** δ (ppm) = 17.1 (C_{F6}), 22.6 (C_{Cy4} or C_{Cy5}), 22.7 (CH_3CONH-), 24.5 (C_{Cy4} or C_{Cy5}), 25.6 (C_{Cy6}), 29.3 (CH_{2Trp}), 30.7 (C_{Cy3}), 46.4 (C_{Cy1}), 49.1 (C_{Cy2}), 56.1 (CH_{Trp}), 68.0 (C_{F2}), 68.6 (C_{F5}), 71.4 (C_{F3}), 73.3 (C_{F4}), 78.3 (C_{F1}), 111.1 (C_{ArTrp}), 112.3 (CH_{ArTrp}), 119.4 (CH_{ArTrp}), 119.8 (CH_{ArTrp}), 120.4 (CH_{ArTrp}), 122.5 (CH_{ArTrp}), 124.5 (CH_{ArTrp}), 128.9 (C_{ArTrp}), 138.1 (C_{ArTrp}), 173.1 (C=O), 173.2 (C=O), 177.3 (C=O). R_f = 0.30 (4:1 $CHCl_3$:MeOH). ESI-MS: *m/z* = 539.4 [$(M+Na)^+$, 100%]. HR-MS (ESI): calculated for $C_{26}H_{36}N_4O_7$ $[M+Na]^+$: 539.24726; found $[M+Na]^+$: 539.24754.

***N*-[(1*S*,2*R*)-2-(D-*N'*-Acetyl-phenylalanyl)cyclohexanecarboxyl]-α-L-fucopyranosylamine (3h)**

Compound **5**[13] was coupled with D-N-acetyl-phenylalanine using the general HBTU procedure. The crude was purified by flash chromatography (1:9 hexane: AcOEt, R_f = 0.33, 88% yield). Zemplen deprotection and flash chromatography (85:15 $CHCl_3$: MeOH, R_f = 0.32) afforded **3h** (quant)**. ^{1}H-NMR (400 MHz,**

CD_3OD) : δ (ppm) = 1.16 (d, 1H, $J_{5\text{-}6}$ = 6.4 Hz, H_{F6}), 1.48-1.27 (m, 4H, CH_{2Cy}), 1.70-1.54 (m, 2H, CH_{2Cy}), 1.83-1.71 (m, 2H, CH_{2Cy}), 1.91 (s, 3H, CH_3CONH-), 2.72-2.65 (m, 1H, H_{Cy1}), 2.85 (dd, 1H, *J* = 13.7 & 8.6 Hz, CH_{2Phe}), 3.08 (dd, 1H, *J* = 13.7 & 6.4 Hz, CH_{2Phe}), 3.62 (d, 1H, $J_{3\text{-}4}$ = 2.3 Hz, H_{F4}), 3.79-3.71 (m, 2H, H_{F3}, H_{F5}), 3.93 (dd, 1H, $J_{2\text{-}3}$ = 10.3, $J_{1\text{-}2}$ = 5.6 Hz, H_{F2}), 4.22-4.14 (m, 1H, H_{Cy2}), 4.60 (dd, 1H, *J* = 8.5 & 6.5 Hz, CH_{Phe}), 5.47 (d, 1H, $J_{1\text{-}2}$ = 5.6 Hz, H_{F1}), 7.29-7.16 (m, 5H, $5H_{ArPhe}$); **^{13}C-NMR (100 MHz, CD_3OD) :** δ (ppm) = 17.1 (C_{F6}), 22.6 (CH_3CONH-), 22.7 (C_{Cy5}), 24.5 (C_{Cy4}), 25.6 (C_{Cy6}), 30.9 (C_{Cy3}), 39.3 (CH_{2Phe}), 46.4 (C_{Cy1}), 49.1 (C_{Cy2}), 56.4 (CH_{Phe}), 68.0 (C_{F2}), 68.6 (C_{F5}), 71.4 (C_{F3}), 73.3 (C_{F4}), 78.3 (C_{F1}), 127.8 (CH_{ArPhe}), 129.5 ($2\times CH_{ArPhe}$), 130.3 ($2\times CH_{ArPhe}$), 138.6 (C_{ArPhe}), 172.7 (C=O), 173.1 (C=O), 177.3 (C=O). R_f = 0.41 (4:1 $CHCl_3$:MeOH). ESI-MS: *m/z* = 500.4 [$(M+Na)^+$, 100%]. HR-MS (ESI): calculated for $C_{24}H_{35}N_3O_7$ $[M+Na]^+$: 500.23672; found $[M+Na]^+$: 500.23646.

***N*-[(1*S*,2*R*)-2-(2-Aminobenzamido)cyclohexanecarboxyl]- α-L-fucopyranosylamine 3i**

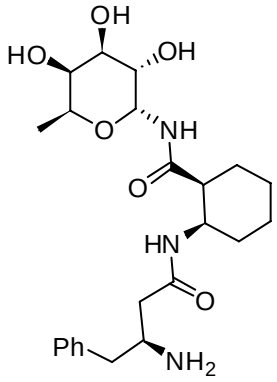


Compound **5** was coupled with *N*-2-Boc-aminobenzoic acid using the general HBTU procedure (see Supplementary Information) and the product (1:1 hexane: AcOEt, R_f = 0.42) was purified by automated chromatography (55 % yield). The amide was dissolved in a mixture of CH_2Cl_2/TFA (1.5 mL, 5/1). The reaction mixture was stirred at r.t. during 2 h and was concentrated under vacuum. Zemplen deprotection of this crude and flash chromatography (8:2 $CHCl_3$: MeOH, R_f = 0.25) afforded the title product (97%).

^{1}H-NMR (400 MHz, CD_3OD): δ (ppm) = 1.02 (d, 3H, $J_{5\text{-}6}$ = 6.3 Hz, H_6), 1.22-2.06 (m, 8H, CH_{2cycl}), 2.84 (m, 1H, H_9), 3.61 (pseudo-d, 1H, $J_{3\text{-}4}$ = 2.6 Hz, H_4), 3.75-3.81 (m, 2H, H_3, H_5), 3.96 (dd, 1H, $J_{1\text{-}2}$ = 5.7 Hz, $J_{2\text{-}3}$ = 10.2 Hz, H_2), 4.52 (m, 1H, H_{10}), 5.50 (m, 1H, H_1), 5.99 (s, 1H, -CH(OAc)), 7.03 (d, 1H, $J_{10\text{-}NH}$ = 8.6 Hz, NH_{11}), 7.08 (d, 1H, NH_7), 7.10-7.82 (m, 4H, H_{Ar}). **^{13}C-NMR (100 MHz, CD_3OD):** δ (ppm) = 16.06 (C_6), 22.22, 24.86, 25.15, 30.90 ($4xCH_{2cyl}$), 46.96 (C_9), 49.37 (C_{10}), 67.88 (C_5), 68.56 (C_2), 71.46

(C_3), 73.36 (C_4), 78.28 (C_1), 177.97 (2xC=O). ESI-MS: *m/z* = 407 [$(M+Na)^+$, 100%]. R_f = 0.25 ($CHCl_3$:MeOH 4:1).

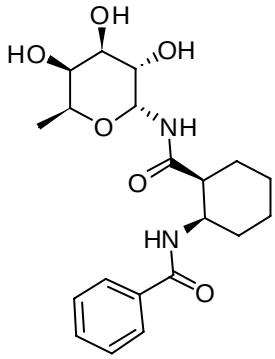
_N_-[(1_S_,2_R_)-2-(L-Homophenylalanyl)cyclohexancarboxyl]- α-L-fucopyranosylamine 3j



Compound **5** was coupled with *N*-Boc-homophenylalanine using the general HBTU procedure (see Supplementary Information) and the product (R_f = 0.75, AcOEt) was isolated by automated chromatography (72 % yield). The amide was dissolved in a mixture of CH_2Cl_2/TFA (1.5 mL, 5/1). The reaction mixture was stirred at r.t. during 2 h and was concentrated under vacuum. Zemplen deprotection of this crude and flash chromatography (8:2 $CHCl_3$: MeOH, R_f = 0.2) afforded the title product (75%).

^{1}H-NMR (400 MHz, D_2O): δ (ppm) = 1.16 (d, 3H, $J_{5\text{-}6}$ = 6.5 Hz, H_6), 1.44-1.76 (m, 8H, CH_{2cycl}), 2.68 (dd, 1H, J_{gem} = 16.0 Hz, $J_{CH2\text{-}CH}$ = 7.5 Hz, -C*H*H'CHNH$_2$-), 2.76 (dd, 1H, $J_{CH2\text{-}CH}$ = 7.5 Hz, -CH*H'*CHNH$_2$-), 2.85 (m, 1H, H_9), 3.10 (d, 2H, $J_{CH\text{-}CH2}$ = 7.4 Hz, -CHCH_2Ph), 3.83-3.87 (m, 2H, H_4, H_5), 3.92 (dd, 1H, $J_{2\text{-}3}$ = 10.6 Hz, $J_{3\text{-}4}$ = 3.4 Hz, H_3), 3.97 (m, 1H, -C*H*CH_2Ph), 4.07 (dd, 1H, $J_{1\text{-}2}$ = 5.7 Hz, H_2), 4.46 (m, 1H, H_{10}), 5.57 (m, 1H, H_1), 7.40-7.55 (m, 5H, H_{Ar}). **^{13}C-NMR (100 MHz, D_2O):** δ (ppm) = 16.48 (C_6), 20.80, 23.11, 23.43, 30.47 (4xCH_{2cyl}), 36.98 (-CH*C*H_2Ph), 38.46 (-*C*H_2CHNH$_2$-), 46.18 (C_9), 48.20 (C_{10}), 50.98 (-CH_2*C*HNH$_2$-), 66.66 (C_2), 68.01 (C_5), 70.19 (C_3), 72.11 (C_4), 77.12 (C_1), 128.38, 129.85, 130.10 (5xC_{Ar}), 135.79 (C_{ipso}), 171.46, 178.42 (2xC=O). ESI-MS: *m/z* = 450.5 [$(M+1)^+$, 100%]. R_f = 0.20 ($CHCl_3$:MeOH 4:1).

_N_-[(1_S_,2_R_)-2-(Benzamido)cyclohexanecarboxyl]- α-L-fucopyranosylamine 3k

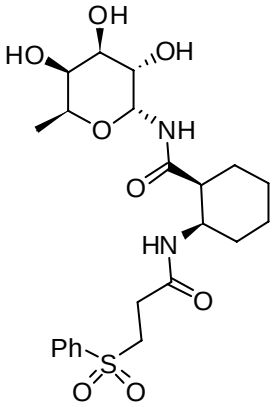


Compound **5** was coupled with benzoic acid using the general acid chloride procedure (see Supplementary Information) and the product (R_f = 0.87, AcOEt) was isolated by automated chromatography (80 % yield). Zemplen deprotection

and flash chromatography (8:2 $CHCl_3$: MeOH, R_f = 0.17) afforded the title product (quant).

^{1}H-NMR (400 MHz, CD_3OD): δ (ppm) = 0.73 (d, 3H, $J_{5\text{-}6}$ = 6.4 Hz, H_6), 1.13-2.06 (m, 8H, CH_{2cycl}), 2.83 (m, 1H, H_9), 3.42 (pseudo-d, 1H, $J_{3\text{-}4}$ = 2.6 Hz, H_4), 3.47 (m, 1H, H_5), 3.64 (dd, 1H, $J_{2\text{-}3}$ = 10.3 Hz, $J_{3\text{-}4}$ = 3.3 Hz, H_3), 3.82 (dd, 1H, $J_{1\text{-}2}$ = 5.6 Hz, H_2), 4.30 (m, 1H, H_{10}), 5.37 (m, 1H, H_1), 7.33-7.43 (m, 3H, H_{Ar}), 7.65-7.72 (m, 2H, H_{Ar}). **^{13}C-NMR (100 MHz, CD_3OD):** δ (ppm) = 16.86 (C_6), 23.22, 24.44, 26.04, 30.84 (4xCH_{2cyl}), 46.06 (C_9), 50.32 (C_{10}), 68.00 (C_2), 68.36 (C_5), 71.54 (C_3), 73.36 (C_4), 78.50 (C_1), 170.14, 177.97 (2xC=O). ESI-MS: *m/z* = 415 [$(M+Na)^+$, 20%]. R_f = 0.17 ($CHCl_3$:MeOH 4:1).

***N*-[(1*S*,2*R*)-2-(3-(Phenylsulfonyl)propanamido)cyclohexancarboxyl)- α-L-fucopyranosylamine 3l**

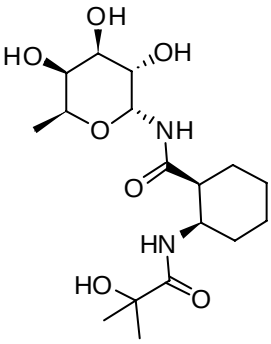


Compound **5** was coupled with (phenylsulfonyl)propionic acid using the general acid chloride procedure (see Supplementary Information) and the product (R_f = 0.59, 1:4 hexane:AcOEt) was isolated by automated chromatography (47 % yield). Zemplen deprotection and flash chromatography (8:2 $CHCl_3$: MeOH, R_f = 0.15) afforded the title product (quant).

^{1}H-NMR (400 MHz, D_2O): δ (ppm) = 1.12 (3H, d, $J_{5\text{-}6}$ = 6.5 Hz, H_6), 1.30-1.82 (m, 8H, CH_{2CYCL}), 2.68-2.82 (m, 3H, H_9, -CH_2SO_2Ph), 3.65 (m, 1H, -C*H*H'CH_2SO_2Ph), 3.76-3.82 (m, 3H, H_4, H_5, -CH*H'*CH_2SO_2Ph), 3.91 (dd, 1H, $J_{2\text{-}3}$ = 10.5 Hz, $J_{3\text{-}4}$ = 3.4 Hz, H_3), 4.08 (dd, 1H, $J_{1\text{-}2}$ = 5.7 Hz, H_2), 5.56 (d, 1H, H_1), 7.75-8.01 (m, 5H, H_{Ar}). **^{13}C-NMR (100 MHz, D_2O):** δ (ppm) = 16.40 (C_6), 21.11, 23.9 (3xCH_{2CYCL}), 29.34 (-CH_2SO_2Ph), 30.27 (CH_{2CYCL}), 45.63 (C_9), 48.68 (C_{10}), 51.75 (-*C*$H_2CH_2SO_2Ph$), 66.64 (C_2), 67.58 (C_5), 69.86 (C_3), 72.09 (C_4), 77.24 (C_1), 128.57, 130.45, 135.65 (3xC_{Ar}), 137.10 (C_{ipso}), 171.00 (C_{12}), 178.33 (C_8). ESI-MS: *m/z* = 485 [$(M+1)^+$, 25%]. R_f = 0.15 ($CHCl_3$:MeOH 4:1).

Supplementary Information

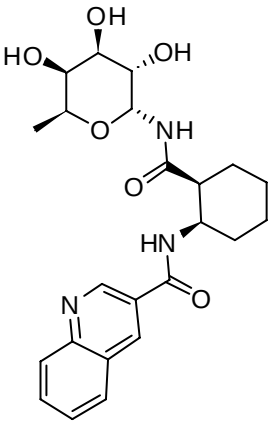
_N_-[(1_S_,2_R_)-2-(2-Hydroxy-2-methylpropanamido)cyclohexancarboxyl]- α-L-fucopyranosylamine 3m



Compound **5** was coupled with 2-acetoxy2-methylpropanoic acid using the general acid chloride procedure (see Supplementary Information) and the product (R_f = 0.59, 1:4 hexane:AcOEt) was isolated by automated chromatography (46 % yield). Zemplen deprotection and flash chromatography (8:2 $CHCl_3$: MeOH, R_f = 0.15) afforded the title product (95%).

^{1}H-NMR (400 MHz, CD_3OD): δ (ppm) = 1.17 (d, 3H, $J_{5\text{-}6}$ = 6.4 Hz, H_6), 1.36 (s, 6H, -C(CH_3)$_2$), 1.31-2.03 (m, 8H, CH_{2cycl}), 2.80 (m, 1H, H_9), 3.64 (m, 1H, H_4), 3.76 (m, 1H, H_5), 3.79 (dd, 1H, $J_{2\text{-}3}$ = 10.3 Hz, $J_{3\text{-}4}$ = 3.4 Hz, H_3), 3.96 (dd, 1H, $J_{1\text{-}2}$ = 5.6 Hz, H_2), 4.14 (m, 1H, H_{10}), 5.50 (d, 1H, H_1). **^{13}C-NMR (100 MHz, CD_3OD):** δ (ppm) = 15.61 (C_6), 21.46, 23.00, 24.96, 29.46 (4xCH_{2cyl}), 26.35, 26.46 (2x-C(*C*H_3)$_2$), 44.84 (C_9, C_{10}), 66.55 (C_2), 67.00 (C_5), 70.03 (C_3), 71.91 (C_4), 73.2 (-*C*(CH_3)$_2$), 76.88 (C_1), 177.39, 178.89 (2xC=O). ESI-MS: *m/z* = 397 [$(M+Na)^+$, 38%]. R_f = 0.15 ($CHCl_3$:MeOH 4:1).

_N_-[(1_S_,2_R_)-2-(Quinoline-3-carboxamido)cyclohexanecarboxyl]- α-L-fucopyranosylamine 3n

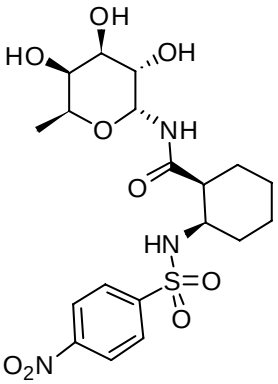


Compound **5** was coupled with quinoline-3-carboxylic acid using the general acid chloride procedure and the product (R_f = 0.45, 1:4 hexane:AcOEt) was isolated by automated chromatography (48 % yield). Zemplen deprotection and flash chromatography (8:2 $CHCl_3$: MeOH, R_f = 0.22) afforded the title product (quant).

^{1}H-NMR (400 MHz, CD_3OD): δ (ppm) = 0.74 (d, 3H, $J_{5\text{-}6}$ = 6.4 Hz, H_6), 11.46-2.15 (m, 8H, CH_{2cycl}), 2.96 (m, 1H, H_9), 3.53 (m, 1H, H_4), 3.61 (m, 1H, H_5), 3.77 (dd, 1H, $J_{2\text{-}3}$ = 10.3 Hz, $J_{3\text{-}4}$ = 3.3 Hz, H_3), 3.93 (dd, 1H, $J_{1\text{-}2}$ = 5.6 Hz, H_2), 4.57 (m, 1H, H_{10}), 5.50 (d, 1H, H_1), 7.72 (m, 1H, H_{19}), 7.91 (m, 1H, H_{18}), 8.08, 8.10 (2xm, 2H, H_{17}, H_{20}), 8.78 (m, 1H, H_{22}), 9.20 (m, 1H, H_{14}). **^{13}C-NMR (100 MHz, CD_3OD):** δ (ppm) = 16.89 (C_6), 22.91, 24.65, 25.55, 31.12 (4xCH_{2cyl}), 46.30 (C_9), 50.34 (C_{10}), 68.00 (C_2), 68.38 (C_5), 71.55 (C_3), 73.30 (C_4), 78.46 (C_1), 128.58 (C_{21}), 129.15 (C_{13}), 129.06, 129.32, 130.45, 132.96, 138.02 (C_{17}, C_{18}, C_{19}, C_{20}, C_{22}), 149.82 (C_{16}), 150.22 (C_{14}), 168.02 (C_{12}), 177.73 (C_8). ESI-MS: *m/z* = 444 [$(M+H)^+$, 100%]. R_f = 0.22 ($CHCl_3$:MeOH 4:1).

Supplementary Information

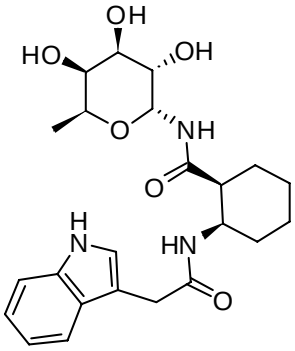
***N*-[(1*S*,2*R*)-2-(4-Nitrobenzenesulfonamido)cyclohexanecarboxyl)-α-L-fucopyranosylamine 3o**



Compound **5** was coupled with 4-nitrobenzenesulfonyl chloride and the product (R_f = 0.68, 1:4 hexane:AcOEt) was isolated by automated chromatography (69 % yield). Zemplen deprotection and flash chromatography (8:2 $CHCl_3$: MeOH, R_f = 0.21) afforded the title product (63%).

^{1}H-NMR (400 MHz, CD_3OD): δ (ppm) = 1.19 (d, 3H, $J_{5\text{-}6}$ = 6.4 Hz, H_6), 1.31-1.86 (m, 8H, CH_{2cycl}), 2.73 (m, 1H, H_9), 3.68-3.72 (m, 2H, H_4, H_{10}), 3.79 (dd, 1H, $J_{2\text{-}3}$ = 10.3 Hz, $J_{3\text{-}4}$ = 3.4 Hz, H_3), 3.93 (m, 1H, H_5), 3.96 (dd, 1H, $J_{1\text{-}2}$ = 5.6 Hz, H_2), 5.50 (d, 1H, H_1), 8.14, 8.41 (2xd 4H, J = 8.4 Hz, H_{Ar}). **^{13}C-NMR (100 MHz, CD_3OD):** δ (ppm) = 16.88 (C_6), 22.62, 23.97, 26.11, 30.85 (4xCH_{2cyl}), 47.24 (C_9), 53.91 (C_{10}), 68.01 (C_2), 68.50 (C_5), 71.48 (C_3), 73.29 (C_4), 78.23 (C_1), 125.35, 129.41 (4xC_{Ar}), 148.74, 151.33 (2xC_{ipso}), 177.00 (2xC=O). ESI-MS: *m/z* = 474 [$(M+H)^+$, 78%]. R_f = 0.21 ($CHCl_3$:MeOH 4:1).

***N*-[(1*S*,2*R*)-2-(3-Indolacetamido)cyclohexanecarboxyl)- α-L-fucopyranosylamine 3p**

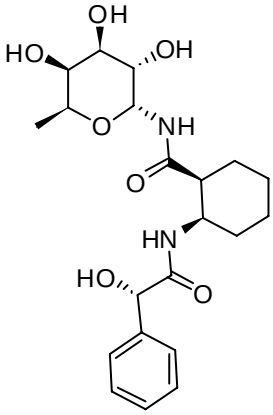


Compound **5** was coupled with 3-indolacetic acid acid using the general HBTU procedure and the product (R_f = 0.68, AcOEt) was isolated by automated chromatography (48 % yield). Zemplen deprotection and flash chromatography (8:2 $CHCl_3$: MeOH, R_f = 0.11) afforded the title product (quant).

^{1}H-NMR (400 MHz, CD_3OD): δ (ppm) = 1.14 (d, 3H, $J_{5\text{-}6}$ = 6.4 Hz, H_6), 1.30-1.84 (m, 8H, CH_{2cycl}), 2.84 (m, 1H, H_9), 3.74-3.91 (m, 5H, CH_{2INDOL}, H_3, H_4, H_5), 4.07 (dd, 1H, $J_{1\text{-}2}$ = 5.7 Hz, $J_{2\text{-}3}$ = 10.6 Hz, H_2), 4.39 (m, 1H, H_{10}), 5.56 (d, 1H, H_1), 7.24-7.39 (m, 3H, H_{Ar}), 7.61 (d, 1H, J = 8.2 Hz, H_{Ar}), 7.70 (d, 1H, J = 7.9 Hz, H_{Ar}). **^{13}C-NMR (100 MHz, CD_3OD):** δ (ppm) = 16.50 (C_6), 21.01, 23.62, 23.81, 30.55 (4xCH_{2cyl}), 33.22 (CH_{2INDOL}), 45.73 (C_9), 48.81 (C_{10}), 66.80 (C_2), 67.96 (C_5), 70.34 (C_3), 72.23 (C_4), 77.46 (C_1), 108.38 ($C_{ipso\text{-}14}$), 112.67, 119.25, 120.28,

122.88, 125.60 (5xC_{Ar}), 128.56, 137.07 (2xC_{ipso}), 174.84 (C_{12}), 178.39 (C_8). ESI-MS: *m/z* = 446.3 [$(M+H)^+$, 100%].. R_f = 0.11 ($CHCl_3$:MeOH 4:1).

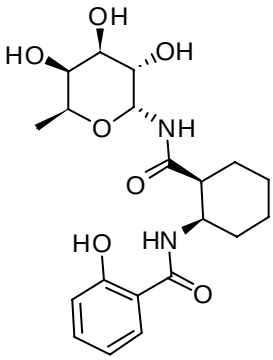
***N*-[(1*S*,2*R*)-2-((*S*)-2-Hydroxyphenylacetamido)cyclohexanecarboxyl]- α-L-fucopyranosylamine 3q**



Compound **5** was coupled with (*S*)-(+)-α-acetoxyphenylacetic acid using the general acid chloride procedure and the product (R_f = 0.38, 1:1 hexane:AcOEt) was isolated by automated chromatography (47 % yield). Zemplen deprotection and flash chromatography (8:2 $CHCl_3$: MeOH, R_f = 0.72) afforded the title product (quant).

^{1}H-NMR (400 MHz, D_2O): δ (ppm) = 1.18 (d, 3H, $J_{5\text{-}6}$ = 6.4 Hz, H_6), 1.40-1.93 (m, 8H, CH_{2cycl}), 2.94 (m, 1H, H_9), 3.78-3.81 (m, 2H, H_4, H_5), 3.93 (dd, 1H, $J_{2\text{-}3}$ = 10.6 Hz, $J_{3\text{-}4}$ = 3.4 Hz, H_3), 4.06 (dd, 1H, $J_{1\text{-}2}$ = 5.7 Hz, H_2), 4.38 (m, 1H, H_{10}), 5.21 (s, 1H, -C*H*(OH)Ph), 5.58 (d, 1H, H_1), 7.45-7.52 (m, 5H, H_{Ar}). **^{13}C-NMR (100 MHz, D_2O):** δ (ppm) = 16.29 (C_6), 20.71, 23.36, 23.67, 30.25 (4xCH_{2cyl}), 45.44 (C_9), 48.41 (C_{10}), 66.47 (C_2), 67.82 (C_5), 70.07 (C_3), 71.97 (C_4), 74.52 (-*C*H(OH)Ph), 77.14 (C_1), 127.61, 129.58 (5xC_{Ar}), 139.16 (C_{ipso}), 174.42, 178.25 (2xC=O). ESI-MS: *m/z* = 405.5 [$(M-OH)^+$, 25%]. R_f = 0.72 ($CHCl_3$:MeOH 4:1).

***N*-((1*S*,2*R*)-2-(2-Hydroxybenzamido)cyclohexanecarboxyl)- α-L-fucopyranosylamine 3r**



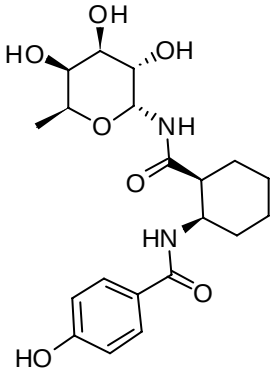
Compound **5** was coupled with 2-acetoxybenzoic acid using the general acid chloride procedure and the product (R_f = 0.3, 1:1 hexane:AcOEt) was isolated by automated chromatography (50 % yield). Zemplen deprotection and flash chromatography (8:2 $CHCl_3$: MeOH, R_f = 0.75) afforded the title product (quant).

^{1}H-NMR (400 MHz, D_2O): δ (ppm) = 0.78 (d, 3H, $J_{5\text{-}6}$ = 6.5 Hz, H_6), 1.48-2.05 (m, 8H, CH_{2cycl}), 3.00 (m, 1H, H_9), 3.61 (dq, 1H, $J_{4\text{-}5}$ < 1 Hz, H_5), 3.67 (dd, 1H, $J_{3\text{-}4}$ = 3.4 Hz, H_4), 3.83 (dd, 1H, $J_{2\text{-}3}$ = 10.6 Hz, H_3), 4.00 (dd, 1H, $J_{1\text{-}2}$ = 5.6 Hz, H_2), 4.56 (m, 1H, H_1), 5.48 (d, 1H, H_1), 7.08, 7.49, 7.84 (3xm, 4H, H_{Ar}). **^{13}C-NMR (100 MHz, D_2O):** δ (ppm) = 16.10 (C_6), 21.62,

23.90, 24.21, 30.39 (4xCH_{2cyl}), 45.59 (C_9), 49.58 (C_{10}), 66.82 (C_2), 67.89 (C_5), 70.43 (C_3), 72.27 (C_4), 77.66 (C_1), 117.96 (C_{Ar}), 118.20 (C_{ipso}), 121.31, 130.36, 134.99 (3xC_{Ar}), 157.28 (C_{ipso}), 169.07, 178.63 (2xC=O). ESI-MS: *m/z* = 431.5 [$(M+Na)^+$, 30%]. R_f = 0.75 ($CHCl_3$:MeOH 4:1).

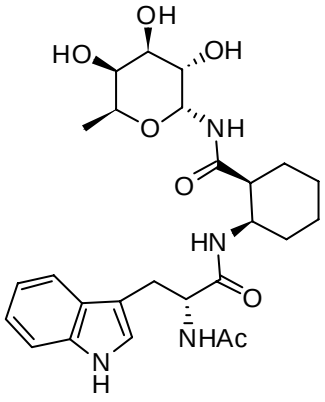
_N_-[(1 _S_,2_R_)-2-(4-Hydroxybenzamido)cyclohexanecarboxyl]- α-L -fucopyranosylamine 3s

Compound **5** was coupled with 4-acetoxybenzoic acid using the general acid chloride procedure and the product (R_f = 0.30, 1:1 hexane:AcOEt) was isolated by automated chromatography (55 % yield). Zemplen deprotection and flash chromatography (8:2 $CHCl_3$: MeOH, R_f = 0.46) afforded the title product (quant).



^{1}H-NMR (400 MHz, D_2O): δ (ppm) = 0.66 (d, 3H, $J_{5\text{-}6}$ = 6.5 Hz, H_6), 1.31-1.95 (m, 8H, CH_{2cycl}), 2.94 (m, 1H, H_9), 3.46 (m, 1H, H_5), 3.59 (pseudo-d, 1H, $J_{3\text{-}4}$ = 3.4 Hz, H_4), 3.76 (dd, 1H, $J_{2\text{-}3}$ = 10.6 Hz, H_3), 3.92 (dd, 1H, $J_{1\text{-}2}$ = 5.7 Hz, H_2), 4.40 (m, 1H, H_{10}), 5.42 (d, 1H, H_1), 6.91, 7.60 (2xd, 4H, H_{Ar}). **^{13}C-NMR (100 MHz, D_2O):** δ (ppm) = 16.04 (C_6), 21.58, 23.57, 23.92, 30.25 (4xCH_{2cyl}), 45.37 (C_9), 49.758 (C_{10}), 66.67 (C_5), 67.82 (C_2), 70.27 (C_3), 72.15 (C_4), 77.52 (C_1), 116.09 (2xC_{Ar}), 126.46 (C_{ipso}), 130.38 (2xC_{Ar}), 159.96 (C_{ipso}), 170.88, 178.75 (2xC=O). ESI-MS: *m/z* = 431.5 [$(M+Na)^+$, 30%]. R_f = 0.46 ($CHCl_3$:MeOH 4:1).

_N_-[(1_S_,2_R_)-2-(D-_N_-Acetyl-Tryptophanoyl**)cyclohexanecarboxyl]- α-L-fucopyranosylamine 3t**



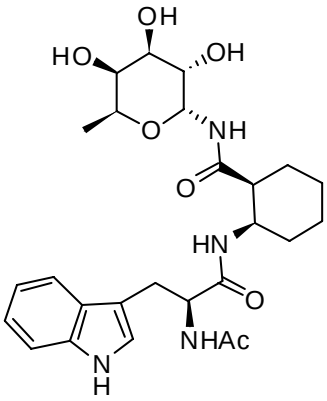
Compound **5** was coupled with N-acetyl-D-tryptophan using the general HBTU procedure and the product (R_f = 0.48, 1:9 hexane:AcOEt) was isolated by automated chromatography (85 % yield). Zemplen deprotection and flash chromatography (4:1 $CHCl_3$: MeOH, R_f = 0.22) afforded the title product (quant.).

^{1}H-NMR (400 MHz, CD_3OD): δ (ppm) = 1.17 (d, 1H, *J*=6.5 Hz, 3H_{6F}), 1.36-

1.12(m 4H, CH_{2cycl}), 1.73-1.54 (m, 4H, CH_{2cycl}), 1.95 (s, 3H, CH_3CONH-), 2.70-2.63 (m, 1H, H_1), 3.09 (dd, 1H, *J*=14.4 & 7.4 Hz, CH_{2Trp}), 3.23 (dd, 1H, *J*=14.4 & 7.2 Hz, CH_{2Trp}), 3.64 (d, 1H, *J*=3.0 Hz, H_{4F}), 3.80-3.74 (m, 2H, *J*=2.8 Hz, H_{3F} + H_{5F}), 3.95 (dd, 1H, *J*=10.3 & 5.6 Hz, H_{2F}), 4.16-4.10 (m, 1H, H_2), 4.66 (t, 1H, *J*=7.3 Hz, CH_{Trp}), 5.48 (d, 1H, *J*=5.6 Hz, H_{1F}), 7.02 (t, 1H, *J*=7.0 Hz, CH_{ArTrp}), 7.12-7.06 (m, 2H, $2CH_{ArTrp}$), 7.33 (d, 2H, *J*=8.1 Hz, CH_{ArTrp}), 7.60 (d, 1H, *J*=7.8 Hz, CH_{ArTrp}). **^{13}C-NMR (100 MHz, CD_3OD):** δ (ppm) = 17.1 (C_{6F}), 22.6 (C_4 or C_5), 22.7 (CH_3CONH-), 24.5 (C_4 or C_5), 25.6 (C_6), 29.3 (CH_{2Trp}), 30.7 (C_3), 46.4 (C_1), 49.1 (C_2), 56.1 (CH_{Trp}), 68.0 (C_{2F}), 68.6 (C_{5F}), 71.4 (C_{3F}), 73.3 (C_{4F}), 78.3 (C_{1F}), 111.1 (C_{ArTrp}), 112.3 (CH_{ArTrp}), 119.4 (CH_{ArTrp}), 119.8 (CH_{ArTrp}), 120.4 (CH_{ArTrp}), 122.5 (CH_{ArTrp}), 124.5 (CH_{ArTrp}), 128.9 (C_{ArTrp}), 138.1 (C_{ArTrp}), 173.1 (C=O), 173.2 (C=O), 177.3 (C=O). ESI-MS: *m/z* = 539.4 [$(M+Na)^+$, 100%].

***N*-[(1 *S*,2*R*)-2-(L-*N*-Acetyl-tryptophanoyl)cyclohexanecarboxyl]- α-L-fucopyranosylamine 3u**

Compound **5** was coupled with *N*-acetyl-L-tryptophan using the general HBTU procedure and the product



(R_f = 0.26, 1:9 hexane:AcOEt) was isolated by automated chromatography (71% yield). Zemplen deprotection and flash chromatography (4:1 $CHCl_3$: MeOH, R_f = 0.32) afforded the title product (quant.).

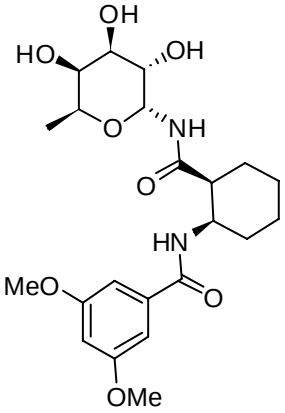
^{1}H-NMR (400 MHz, CD_3OD): δ (ppm) = 1.10 (d, 1H, *J*=6.4 Hz, $3H_{6F}$), 1.73-1.23 (m, 7H, H_3 + $2H_4$ + $2H_5$ + $2H_6$), 1.87 (s, 3H, CH_3CONH-), 2.03-1.81 (m, 1H, H_3), 2.75-2.69 (m, 1H, H_1), 3.06 (dd, 1H, *J*=14.9 & 9.1 Hz, CH_{2Trp}), 3.22 (dd, 1H, *J*=14.9 & 4.8 Hz, CH_{2Trp}), 3.59 (d, 1H, *J*=3.0 Hz, H_{4F}), 3.79-3.70 (m, 2H, H_{3F} + H_{5F}), 3.93 (dd, 1H, *J*=10.3 & 5.6 Hz, H_{2F}), 4.24-4.16 (m, 1H, H_2), 4.67 (dd, 1H, *J*=9.0 & 4.9 Hz, CH_{Trp}), 5.50 (d, 1H, *J*=5.6 Hz, H_{1F}), 6.99 (t, 1H, *J*=7.0 Hz, CH_{ArTrp}), 7.11-7.04 (m, 2H, $2CH_{ArTrp}$), 7.31 (d, 2H, *J*=8.1 Hz, CH_{ArTrp}), 7.61 (d, 1H, *J*=7.8 Hz, CH_{ArTrp}).

^{13}C-NMR (100 MHz, CD_3OD): δ (ppm) = 17.1 (C_{6F}), 22.5 (C_4 or C_5), 23.0 (CH_3CONH-), 24.4 (C_4 or C_5), 26.3 (C_6), 29.0 (CH_{2Trp}), 30.8 (C_3), 46.4 (C_1), 49.3 (C_2), 55.7 (CH_{Trp}), 68.1 (C_{2F}), 68.6 (C_{5F}), 71.5 (C_{3F}), 73.3 (C_{4F}), 78.3 (C_{1F}), 111.3 (CH_{ArTrp}), 112.2 (CH_{ArTrp}), 119.5 (CH_{ArTrp}), 119.8 (CH_{ArTrp}), 122.4 (CH_{ArTrp}), 124.4

(CH_{ArTrp}), 128.9 (C_{ArTrp}), 138.1 (C_{ArTrp}), 173.3 (C=O), 173.7 (C=O), 177.4 (C=O). ESI-MS: *m/z* = 539.4 [$(M+Na)^+$, 100%].

_N_-[(1_S_,2_R_)-2-(3,5-Dimethoxybenzamido)cyclohexanecarboxyl]-α-L-fucopyranosylamine 3v

Compound **5** was coupled with 3,5-dimethoxybenzoic acid using the general HBTU procedure and the product (R_f = 0.32, 1:1.5 hexane:AcOEt) was isolated by automated chromatography (87 % yield). Zemplen deprotection and flash chromatography (4:1 $CHCl_3$: MeOH, R_f = 0.61) afforded the title product (quant.).



^{1}H-NMR (400 MHz, CD_3OD): δ (ppm) = 0.85 (d, 1H, *J*=6.4 Hz, $3H_{6F}$), 1.81-1.34 (m, 6H, H_3 + $2H_4$ + $2H_5$ + H_6), 2.00-1.90 (m, 1H, H_6), 2.19-2.10 (m, 1H, H_3), 2.93 (td, 1H, *J*=8.5 & 4.4 Hz, H_1), 3.51 (d, 1H, *J*=2.6 Hz, H_{4F}), 3.55 (q, 1H, *J*=6.6 Hz, H_{5F}), 3.73 (dd, 1H, *J*=10.3 & 3.4 Hz, H_{3F}), 3.81 (s, 6H, 2 x OMe), 3.91 (dd, 1H, *J*=10.3 & 5.6 Hz, H_{2F}), 4.37-4.31 (m, 1H, H_2), 5.47 (d, 1H, *J*=5.6 Hz, H_{1F}), 6.61 (t, 1H, *J*=2.2 Hz, H_{Ar}), 6.91 (d, 2H, *J*=2.2 Hz, $2H_{Ar}$). **^{13}C-NMR (100 MHz, CD_3OD):** δ (ppm) = 16.7 (C_{6F}), 23.2 (C_5), 24.2 (C_4), 26.0 (C_6), 30.6 (C_3), 45.8 (C_1), 50.4 (C_2), 56.1 (2 x OMe), 67.9 (C_{2F}), 68.3 (C_{5F}), 71.4 (C_{3F}), 73.3 (C_{4F}), 78.4 (C_{1F}), 104.5 ($1CH_{Ar}$), 106.5 ($2CH_{Ar}$), 162.4 ($2C_{ArOMe}$), 169.9 (C=O), 177.7 (C=O). ESI-MS: *m/z* = 475.3 [$(M+Na)^+$, 100%].

(1_S_,2_S_)-2-Aminocyclohexanecarboxylic acid series: Ligands 11

_N_-((1_S_,2_S_)-2-Acetamido-cyclohexanecarboxyl)-α-L-fucopyranosylamine (11a)

The crude hydrogenation product of **29** (see Supplementary Information – SI-Scheme 3) was used in the general acetylation method (see Supplementary Information). The product was purified by flash chromatography on silica gel (AcOEt, R_f = 0.21). Yield: 16 mg (73 %). The Zemplen deprotection was performed and the product was not further purified. (R_f = 0.10, $CHCl_3$/MeOH 4:1) Yield (**11a**): 6 mg (55 %)

^{1}H-NMR (400 MHz, CD_3OD) : δ (ppm) = 1.17(d, 3H, $J_{5\text{-}6}$ = 6.5 Hz, H_{F6}), 1.21 – 1.35 (m, 2H, H_{Cy3ax} and

H_{Cy5ax}), 1.35 – 1.45 (m, 1H, H_{Cy4ax}), 1.47 – 1.57 (m, 1H, H_{Cy6ax}), 1.71 – 1.79 (m, 2H, H_{Cy4eq} and H_{Cy5eq}), 1.88 (s, 3H, Ac-Me), 1.89 – 1.96 (m, 2H, H_{Cy3eq} and H_{Cy6eq}), 2.36 (td, 1H, $J_{1\text{-}6a}$ = 3.6 Hz, $J_{1\text{-}6b}$ = 11.7 Hz, $J_{1\text{-}2}$ = 11.7 Hz , H_{Cy1}), 3.63 – 3.66 (m, 1H, H_{F4}), 3.73 (dd, $J_{3\text{-}4}$ = 3.4 Hz, $J_{2\text{-}3}$ = 10.3 Hz, 1H, H_{F3}), 3.77 (q, $J_{5\text{-}6}$ = 6.5 Hz ,1H, H_{F5}), 3.87 – 3.96 (m, 2H, H_{C2}, H_{F2}), 5.47 (d, 1H, $J_{1\text{-}2}$ = 5.6 Hz, HF_1) **^{13}C-NMR (100 MHz, CD_3OD) :** δ (ppm) = 17.1 (C_{F6}), 23.0 (Ac-CH_3), 26.1 (C_{Cy4} or C_{Cy5}), 26.2 (C_{Cy4} or C_{Cy5}), 30.9 (C_{Cy6}), 33.8 (C_{Cy3}), 51.2 (C_{Cy2}), 51.7 (C_{Cy1}), 68.1 (C_{F2}), 68.6 (C_{F5}), 71.7 (C_{F3}), 73.3 (C_{F4}), 78.6 (C_{F1}), 172.4 (NHCO), 177.8 (NHCO). HRMS (FT-ICR, ESI): *m/z* calcd for $C_{15}H_{26}N_2O_6$: 353.16831 $[M + Na]^+$; found: 353.16832. $[\alpha]_D$ = -140.8 (c 0.05, MeOH)-

***N*-[(1*S*,2*S*)-2-(3-Hydroxybenzamido)cyclohexanecarboxyl]-α-L-fucopyranosylamine (11b)**

The crude hydrogenation product of **29** (see Supplementary Information – SI-Scheme 3) was coupled with 3-hydroxybenzoic acid using the HBTU general procedure (see Supplementary Information) and the product was purified by flash chromatography (AcOEt, R_f = 0.15, 71% yield). Zemplen deprotection and flash chromatography (4:1 chloroform:methanol, R_f = 0.15) afforded **11b**. **^{1}H-NMR (400 MHz, CD_3OD) :** δ (ppm) = 0.59 (d, 3H, $J_{5\text{-}6}$ = 6.5 Hz, H_{F6}), 1.25 – 1.30 (m, 1H, H_{Cy4ax} or H_{Cy5ax}), 1.36 – 1.42 (m, 1H, H_{Cy3ax} and H_{Cy4ax} or H_{Cy5ax}), 1.51 – 1.64 (m, 1H, H_{Cy6ax}), 1.69 – 1.79 (m, 2H, H_{Cy4eq} and H_{Cy5eq}), 1.81 – 1.89 (m, 1H, H_{Cy6eq}), 1.91 – 1.98 (m, 1H, H_{Cy3eq}), 2.48 (td, 1H, $J_{1\text{-}6a}$ = 3.5 Hz, $J_{1\text{-}6b}$ = 11.7 Hz, $J_{1\text{-}2}$ = 11.7 Hz, H_{Cy1}), 3.32 – 3.34 (m, 1H, H_{F4}), 3.40 (q, $J_{5\text{-}6}$ = 6.3 Hz, 1H, H_{F5}), 3.62 (dd, 1H, $J_{3\text{-}4}$ = 3.4 Hz, $J_{2\text{-}3}$ = 10.4 Hz, H_{F3}), 3.81 (dd, 1H, $J_{1\text{-}2}$ = 5.6 Hz, $J_{2\text{-}3}$ = 10.3 Hz, H_{F2}), 4.01 – 4.09 (m, 1H, H_{C2}), 5.31 (d, 1H, $J_{1\text{-}2}$ = 5.6 Hz, H_{F1}), 6.74 – 6.78 (m, 1H, H_{Ar}), 7.01 – 7.08 (m, 3H, Ar). **^{13}C-NMR (100 MHz, CD_3OD) :** δ (ppm) = 16.5 (C_{F6}), 25.9 (C_{Cy4} or C_{Cy5}), 26.3 (C_{Cy4} or C_{Cy5}), 30.2 (C_{Cy6}), 33.9 (C_{Cy3}), 51.3 (C_{Cy1}), 52.0 (C_{Cy2}), 67.9 (C_{F2}), 68.6 (C_{F5}), 71.5 (C_{F3}), 73.2 (C_{F4}), 78.8 (C_{F1}), 116.5 (Ar), 116.7 (Ar), 122.3 (Ar), 130.4 (Ar), 136.37 (Cquart., Ar.), 164.59 (Cquart., Ar.), 169.81 (Cquart.), 178.13 (Cquart.). HRMS (FT-ICR, ESI): *m/z* calcd for $C_{20}H_{28}N_2O_7$: 431.17887 $[M + Na]^+$; found: 431.17951. $[\alpha]_D$ = -21.0 (c = 0.25, MeOH).

Supplementary Information

***N*-[(1*S*,2*S*)-2-(3,5-Dihydroxybenzamido)cyclohexanecarboxyl]-α-L-fucopyranosylamine (11c)**

The crude hydrogenation product of **29** (see Supplementary Information – SI-Scheme 3) was coupled with 3,5-dihydroxybenzoic acid using the HBTU general procedure (see Supplementary Information) and the product was purified by flash chromatography (7:3 ethyl acetate:*n*-hexane, R_f = 0.23). Yield: 19 mg (26 %). Zemplen deprotection and flash chromatography (4:1 chloroform:methanol, R_f = 0.14) afforded **11c**. Yield: 9 mg (69 %)- **^{1}H-NMR (400 MHz, CD_3OD) :** δ (ppm) = 0.73 (d, 3H, $J_{5\text{-}6}$ = 6.5 Hz, H_{F6}), 1.28 – 1.46 (m, 3H, H_{Cy5ax}, H_{Cy4ax}, H_{Cy3ax}), 1.51 – 1.61 (m, 1H, H_{Cy6ax}), 1.69 – 1.78 (m, 1H, H_{Cy5eq}, H_{Cy4eq}), 1.84 – 1.90 (m, 1H, H_{Cy6eq}), 1.90 – 1.97 (m, 1H, H_{Cy3eq}), 2.55 (td, $J_{1\text{-}6a}$ = 3.5 Hz, $J_{1\text{-}2}$ = 11.6 Hz, $J_{1\text{-}6b}$ = 11.6 Hz, 1H, H_{Cy1}), 3.40 – 3.42 (m, 1H, H_{F4}), 3.49 (q, $J_{5\text{-}6}$ = 6.5 Hz, 1H, H_{F5}), 3.64 (dd, 1H, $J_{2\text{-}3}$ = 10.3 Hz, $J_{3\text{-}4}$ = 3.4 Hz, H_{F3}), 3.79 (dd, 1H, $J_{1\text{-}2}$ = 5.6 Hz, $J_{2\text{-}3}$ = 10.3 Hz, H_{F2}), 3.99 (td, $J_{2\text{-}3a}$ = 4.0 Hz, $J_{2\text{-}3b}$ = 11.1 Hz, $J_{1\text{-}2}$ = 11.1 Hz, 1H, H_{Cy2}), 5.35 (d, 1H, $J_{1\text{-}2}$ = 5.6 Hz, H_{F1}), 6.35 (t, 1H, J^4 = 2.2 Hz, H_{Ar4}), 6.67 (d, 2H, J^4 = 2.2 Hz, H_{Ar2} and H_{Ar6}). **^{13}C-NMR (100 MHz, CD_3OD) :** δ (ppm) = 16.6 (C_{F6}), 25.9 (C_{Cy5}), 26.3 (C_{Cy4}), 30.4 (C_{Cy6}), 33.5 (C_{Cy3}), 51.1 (C_{Cy1}), 52.3 (C_{Cy2}), 68.0 (C_{F2}), 68.6 (C_{F5}), 71.6 (C_{F3}), 73.3 (C_{F4}), 78.7 (C_{F1}), 106.7 (Ar), 106.9 (Ar), 137.8 (Cquart.) 160.0 (Cquart.), 169.3 (CONH), 178.0 (CONH). HRMS (FT-ICR, ESI): *m/z* calcd for $C_{20}H_{28}N_2O_8$: 447.17379 $[M + Na]^+$; found: 447.17369. $[\alpha]_D$ = -76.2 (c = 0.20, MeOH).

(1*S*,2*S*)-2-Aminocyclohexanecarboxylic acid series: Ligands 12

***N*-[(1*R*,2*R*)-2-(3-Hydroxybenzamido)cyclohexanecarboxyl]-α-L-fucopyranosylamine (12b)**

The crude hydrogenation product of **30** (see Supplementary Information – SI-Scheme 3) was coupled with 3-hydroxybenzoic acid using the HBTU general procedure (see Supplementary Information) and the product was purified by flash chromatography (6:4 ethyl acetate:petroleum ether R_f = 0.17). Yield: 28 mg (53 %) Zemplen deprotection and flash chromatography (85:15 chloroform:methanol, R_f = 0.10) afforded **12b**. Yield: 7 mg (50 %). **^{1}H-NMR (400 MHz, CD_3OD) :** δ (ppm) = 0.93 (d, 3H, $J_{5\text{-}6}$ = 6.5 Hz, H_{F6}), 1.24 – 1.63 (m, 4H, H_{Cy3ax}, H_{Cy6ax} and H_{Cy4} and/or H_{Cy5}), 1.76 – 1.78 (m, 2H, H_{Cy4} and/or H_{Cy5}), 1.93 – 2.02 (m, 2H, H_{Cy3eq} and H_{Cy6eq}), 2.47 (td, 1H, $J_{1\text{-}6b}$ = 3.6 Hz, $J_{1\text{-}2}$ = 11.9 Hz, $J_{1\text{-}6b}$ = 11.9 Hz, H_{Cy1}), 3.54 – 3.55

(m, 1H, H_{F4}), 3.60 (q, J_{5-6} = 6.4 Hz, 1H, H_{F5}), 3.78 (dd, 1H, J_{3-4} = 3.4 Hz, J_{2-3} = 10.4 Hz, H_{F3}), 3.89 (dd, 1H, J_{1-2} = 5.6 Hz, J_{2-3} = 10.4 Hz, H_{F2}), 4.17 (td, J_{2-3} = 4.0 Hz, J_{1-2} = 11.3 Hz, J_{2-3} = 11.3 Hz, 1H, H_{Cy2}), 5.41 (d, 1H, J_{1-2} = 5.7 Hz, H_{F1}), 6.85 – 6.90 (m, 1H, H_{Ar2}), 7.12 – 7.20 (m, 3H, $H_{Ar4,5,6}$). **^{13}C-NMR (100 MHz, CD_3OD) :** δ (ppm) = 16.84 (C_{F6}), 26.22 (C_{Cy4} or C_{Cy5}), 26.42 (C_{Cy4} or C_{Cy5}), 301.70 (C_{Cy6}), 33.78 (C_{Cy3}), 51.00 (C_{Cy2}), 52.25 (C_{Cy1}), 67.99 (C_{F2}), 68.44 (C_{F5}), 71.47 (C_{F3}), 73.32 (C_{F4}), 78.63 (C_{F1}), 115.55 (Ar-CH), 119.52 (Ar-CH), 119.61 (Ar), 130.66 (Ar), 137.31 (Cquart.,), 158.88 (Cquart.), 169.95 (Cquart.), 178.07 (Cquart.). HRMS (FT-ICR, ESI): *m/z* calcd for $C_{20}H_{28}N_2O_7$: 431.17887 $[M + Na]^+$; found: 431.17963. $[\alpha]_D$ = -65.0 (c = 0.20, MeOH) for a sample contained 8% of the beta anomer.

β-Alanine series: Ligands 9

***N*-(*N′*-Acetyl-β-alanyl)-α-L-fucopyranosylamine (9a)**

The crude hydrogenation product of **27** (see Supplementary Information – SI-Scheme 3) was used in the general acetylation method (see Supplementary Information). The product was purified by flash chromatography on silica gel (AcOEt, R_f = 0.17, quant.). Zemplen deprotection and flash chromatography (4:1 $CHCl_3$:MeOH, R_f = 0.2) afforded **9a** (quant.). **^{1}H-NMR (400 MHz, CD_3OD) :** δ (ppm) = 1.90 (d, 3H, J_{6-5} = 5.6 Hz, H_{F6}), 1.93 (s, 3H, $NHC(O)CH_3$), 2.50 (t, 2H, *J* = 6.0 Hz, $C(O)CH_2CH_2NHAc$), 3.43 (t, 2H, *J* = 6.0 Hz, $C(O)CH_2CH_2NHAc$), 3.65 (br s, 1H, H_{F4}), 3.73–3.80 (br s, 2H, H_{F5}, H_{F3}), 3.93–4.10 (m, 1H, H_{F2}), 5.55 (dd, 1H, J_{1-2} = 5.6 Hz, J_{1-NH} = 7.6 Hz, H_{F1}), 8.05 (br s, 1H, $C(O)CH_2CH_2NHAc$), 8.35 (d, 1H, J_{1-NH} = 7.6 Hz, α-NHC(O)); **^{13}C-NMR (100 MHz, CD_3OD) :** δ (ppm) = 15.5 (C_{F6}), 21.1 ($NHC(O)CH_3$), 35.1 ($C(O)CH_2CH_2NHAc$), 35.4 ($C(O)CH_2CH_2NHAc$), 66.5 (C_{F2}), 77.2, 70.0, (C_{F3}, C_{F5}), 72.3 (C_{F4}), 77.1 (C_{F1}), 172.0 (C=O), 173.6 (C=O); R_f = 0.2 (4:1 $CHCl_3$:MeOH). ESI-MS: *m/z* = 277.3 $[(M+H)^+$, 100%].

***N*-[*N′*-(3-Hydroxybenzoyl)-β-alanyl]-α-L-fucopyranosylamine (9b)**

The crude hydrogenation product of **27** (see Supplementary Information – SI-Scheme 3) was coupled with 3-acetoxybenzoic acid using the HBTU general method (see Supplementary Information). The product was

purified by flash chromatography on silica gel (1:4 hexane: AcOEt, R_f = 0.25, 50% yield). Zemplen deprotection and flash chromatography (9:1 $CHCl_3$: MeOH, R_f = 0.17) afforded **9b** (quant.).

^{1}H-NMR (400 MHz, CD_3OD) : δ (ppm) = 1.12 (d, 3H, $J_{6\text{-}5}$ = 6.5 Hz, H_{F6}), 2.70-2.54 (m, 2H, NHOC-CH_2-), 3.68-3.59 (m, 3H, H_{F5} + -*CH_2*NHCO-), 3.76-3.70 (m, 1H, H_{F4}), 3.76 (dd, 1H, $J_{2\text{-}3}$ = 10.4 Hz, $J_{3\text{-}4}$ = 3.5 Hz, H_{F3}), 3.96 (dd, 1H, $J_{2\text{-}3}$ =10.4 Hz, $J_{1\text{-}2}$ = 5.6 Hz, H_{F2}), 5.57 (d, 1H, $J_{1\text{-}2}$ = 5.6 Hz, H_{F1}), 6.96-6.91 (m, 1H, H_{Ar}), 7.27-7.20 (m, 3H, 3xH_{Ar}); **^{13}C-NMR (100 MHz, CD_3OD) :** δ (ppm) = 16.9 (C_{F6}), 36.7 (NHOC-$\underline{CH_2}$-), 37.4 (-$\underline{CH_2}$NHCO-), 68.0 (C_{F2}), 68.6, 71.5 (C_{3F}, C_{4F}), 73.3 (C_{F5}), 78.3 (C_{F1}), 115.3 (CH_{Ar}), 119.1 (CH_{Ar}), 120.8 (CH_{Ar}), 130.6 (CH_{Ar}), 137.0 (C_{Ar}), 159.0 (C_{Ar}), 170.4 (C=O), 175.3 (C=O); R_f = 0.24 (4:1 $CHCl_3$:MeOH)-ESI-MS: *m/z* = 377.5 [$(M+Na)^+$, 100%]. HR-MS (ESI): calculated for $C_{16}H_{21}N_2O_7$ $[M-1]^-$: 353.13542; found $[M-1]^-$: 353.13565.

***N*-[*N'*-(3,5-Dihydroxybenzoyl)-β-alanyl]-α-L-fucopyranosylamine (9c)**

The crude hydrogenation product of **27** (see Supplementary Information – SI-Scheme 3) was coupled with 3,5-diacetoxybenzoic acid using the HBTU general procedure (see Supplementary Information). The product was purified by flash chromatography on silica gel (1:4 hexane: AcOEt, R_f = 0.3, 55% yield). Zemplen deprotection and flash chromatography (85:15 $CHCl_3$: MeOH, R_f = 0.23) afforded **9c** (quant.).

^{1}H-NMR (400 MHz, CD_3OD) : δ (ppm) = 1.12 (d, 3H, $J_{6\text{-}5}$ = 6.5 Hz, H_{F6}), 2.69-2.53 (m, 2H, -NHOC*CH_2*-), 3.65-3.59 (m, 3H, H_{F4} + -*CH_2*NHCO-), 3.80-3.70 (m, 2H, H_{F3}, H_{F5}), 3.96 (dd, 1H, $J_{2\text{-}3}$ =10.3 Hz, $J_{1\text{-}2}$ = 5.6 Hz, H_{F2}), 5.56 (d, 1H, $J_{1\text{-}2}$ =5.6 Hz, H_{1F}), 6.40 (dt, 1H, J = 2.1 & 0.9 Hz, H_{Ar}), 6.71-6.68 (m, 2H, 2H_{Ar}); **^{13}C-NMR (100 MHz, CD_3OD) :** δ (ppm) = 16.9 (C_{F6}), 36.6 (NHOC-$\underline{CH_2}$-), 37.4 (-$\underline{CH_2}$NHCO-), 68.0 (C_{F2}), 68.7, 71.5 (C_{F3}, C_{F5}), 73.3 (C_{F4}), 78.4 (C_{F1}), 116.8 (3×CH_{Ar}), 137.7 (C_{Ar}), 159.9 (2×C_{Ar}), 170.6 (C=O), 175.3 (C=O); R_f = 0.3 (4:1 $CHCl_3$:MeOH). ESI-MS: *m/z* = 393.5 [$(M+Na)^+$, 100%]. HR-MS (ESI): calculated for $C_{16}H_{21}N_2O_8$ $[M-1]^-$: 369.13034; found $[M-1]^-$: 369.13089.

Supplementary Information

_N_-[_N'_-(D-Acetyl-triptophanyl)-β-alanyl]- α -L-fucopyranosylamine (9g)

The crude hydrogenation product of **27** (see Supplementary Information – SI-Scheme 3) was coupled with D-*N*-acetyl-triptophane using the HBTU general procedure (see Supplementary Information). The product was purified by flash chromatography on silica gel (AcOEt, R_f = 0.67, 47% yield). Zemplen deprotection and flash chromatography (85:15 $CHCl_3$: MeOH, R_f = 0.15) afforded **9g** (quant.). **^{1}H-NMR (400 MHz, CD_3OD) :** δ (ppm) = 1.16 (d, 3H, $J_{6\text{-}5}$ = 6.4 Hz, H_{F6}), 1.92 (s, 3H, CH_3CONH-), 2.45-2.27 (m, 2H, NHOC-CH_2-), 3.09 (dd, 1H, J = 14.5 & 7.6 Hz, CH_{2Trp}), 3.22 (dd, 1H, J = 14.4 & 6.5 Hz, CH_{2Trp}), 3.44-3.30 (m, 1H, -CH_2NHCO-), 3.65-3.62 (m, 1H, H_{F4}), 3.81-3.73 (m, 2H, H_{F3}, H_{F5}), 3.95 (dd, 1H, $J_{2\text{-}3}$ = 10.3 Hz, $J_{1\text{-}2}$ = 5.6 Hz, H_{F2}), 4.56 (t, 1H, J = 7.1 Hz, CH_{Trp}), 5.54 (d, 1H, $J_{1\text{-}2}$ = 5.6 Hz, H_{F1}), 7.01 (t, 1H, J = 7.4 Hz, H_{ArTrp}), 7.11-7.05 (m, 2H, $2H_{ArPhe}$), 7.32 (d, 1H, J = 8.0 Hz, H_{ArTrp}), 7.58 (d, 1H, J = 7.8 Hz, H_{ArTrp}); **^{13}C-NMR (100 MHz, CD_3OD) :** δ (ppm) = 16.9 (C_{F6}), 22.6 (CH_3CONH-), 29.0 (CH_{2Trp}), 36.5 (NHOC-$\underline{CH_2}$-), 36.8 (-$\underline{CH_2}$NHCO-), 56.1 (CH_{Trp}), 68.1 (C_{F2}), 68.7, 71.5 (C_{F3}, C_{F5}), 73.3 (C_{F4}), 78.3 (C_{F1}), 101.4 (C_{Ar}), 111.0 (2xC_{Ar}), 112.3 (CH_{Ar}), 119.4 (CH_{Ar}), 119.8 (CH_{Ar}), 122.5 (CH_{Ar}), 124.5 (CH_{Ar}), 128.9 (C_{Ar}), 138.1 (C_{Ar}), 173.2 (C=O), 174.3 (C=O), 175.1 (C=O); R_f = 0.25 ($CHCl_3$:MeOH 4:1). ESI-MS: *m/z* = 485.6 [$(M+Na)^+$, 100%]. HR-MS (ESI): calculated for $C_{22}H_{30}N_4O_7Na$ $[M+Na]^+$: 485.20067; found $[M+Na]^+$: 485.20057.

_N_-[_N'_-(D-_N_-Acetyl-phenylalanyl)-β-alanyl]- α-L-fucopyranosylamine (9h)

The crude hydrogenation product of **27** (see Supplementary Information – SI-Scheme 3) was coupled with D-*N*-acetyl-phenylalanine using the HBTU general procedure (see Supplementary Information). The product was purified by flash chromatography on silica gel (100:2, AcOEt:MeOH, R_f = 0.12, 60% yield). Zemplen deprotection and flash chromatography (9:1 $CHCl_3$: MeOH, R_f = 0.13) afforded **9h** (quant.).

^{1}H-NMR (400 MHz, CD_3OD) : δ (ppm) = 1.17 (d, 3H, $J_{5\text{-}6}$ = 6.5 Hz, H_{6F}), 1.90 (s, 3H, CH_3CONH-), 2.51-2.35 (m, 2H, NHOC-CH_2-), 2.86 (dd, 1H, J = 13.8 & 8.9 Hz, CH_{2Phe}), 3.08 (dd, 1H, J = 13.8 & 6.2 Hz, CH_{2Phe}), 3.50-3.30 (m, 2H, -CH_2NHCO-), 3.66-3-63 (m, 1H, H_{F4}), 3.81-3.74 (m, 2H, H_{F3}, H_{F5}), 3.96 (dd, 1H, $J_{2\text{-}3}$ = 10.3 Hz, $J_{1\text{-}2}$ = 5.6 Hz, H_{F2}), 4.42 (dd, 1H, J = 8.8 & 6.3 Hz, CH_{Phe}), 5.56 (d, 1H, $J_{1\text{-}2}$ = 5.6 Hz, H_{F1}), 7.31-7.17 (m, 5H, $5H_{ArPhe}$); **^{13}C-NMR (100 MHz, CD_3OD) :** δ (ppm) = 17.6 (C_{F6}), 22.4 (CH_3CONH-),

36.7 (NHOC-$\underline{CH_2}$-), 36.8 (-$\underline{CH_2}$NHCO-), 39.0 (CH_{2Phe}), 58.5 (CH_{Phe}), 68.1 (C_{F2}), 68.7, 71.5 (C_{F3}, C_{F5}), 73.3 (C_{F4}), 78.3 (C_{F1}), 127.8 (CH_{Ar}), 129.5 (CH_{Ar}), 130.3 (CH_{Ar}), 138.5 (C_{Ar}), 173.2 (C=O), 173.8 (C=O), 175.1 (C=O); R_f = 0.20 (4:1 $CHCl_3$:MeOH). ESI-MS: *m/z* = 446.5 [$(M+Na)^+$, 100%]. HR-MS (ESI): calculated for $C_{20}H_{29}N_3O_7Na$ $[M+Na]^+$: 446.18977; found $[M+Na]^+$: 446.19005.

1 G. Timpano, G. Tabarani, M. Anderluh, D. Invernizzi, F. Vasile, D. Potenza, P. M. Nieto, J. Rojo, F. Fieschi, A. Bernardi, *ChemBioChem* **2008**, *9*, 1921-1930

2 F. Damkaci, P. DeShong, *J. Am. Chem. Soc.* **2003**, *125*, 4408-4409

3 M. Andreini , M. Anderluh , A. Audfray , A. Bernardi , A. Imberty, *Carb. Res.* **2010**, *345*, 1400-1407

4 a) C. Bolm, I. Schiffers, C. L. Dinter, A. Gerlach, *J. Org. Chem.* **2000**, *65*, 6984-6991; b) A. Bernardi, D. Arosio, D. Dellavecchia, F. Micheli, *Tetrahedron: Asymm.* **1999**, *10*, 3403 – 3407

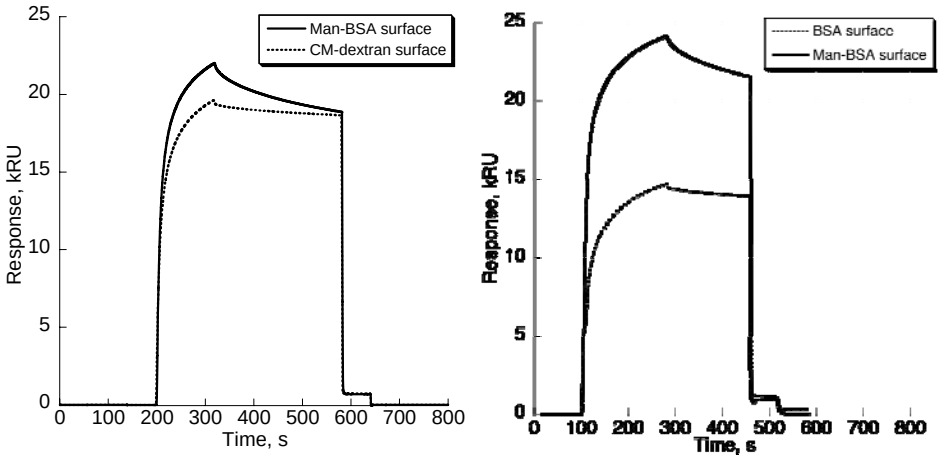
5 M. Adamczyk, J. R. Fishpaugh, *Tetrahedron Lett.* **1996**, *37*, 4305–4308

Supplementary Information

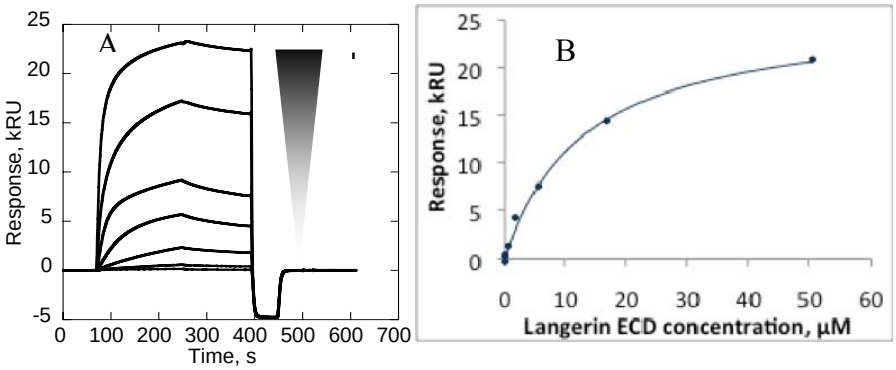
2. Supplementary Information – Surface Plasmon Resonance Experiments

1. Properties of Langerin binding to BSA-Man SPR surfaces and set up of the inhibition test.

As for DC-SIGN, the ability of Langerin to bind to surface functionalized with Man-BSA was tested. In the case of Langerin, strong binding to the reference surface was observed, due to the presence of the dextran polymer (SI-Fig.1). This is limited but not suppressed by using a reference surface functionalized with non-glycosylated BSA (SI-Fig.1). Therefore, the dextran/Man-BSA surface was considered as a combined ligand of Langerin ECD and thus binding responses were not reference surface corrected.

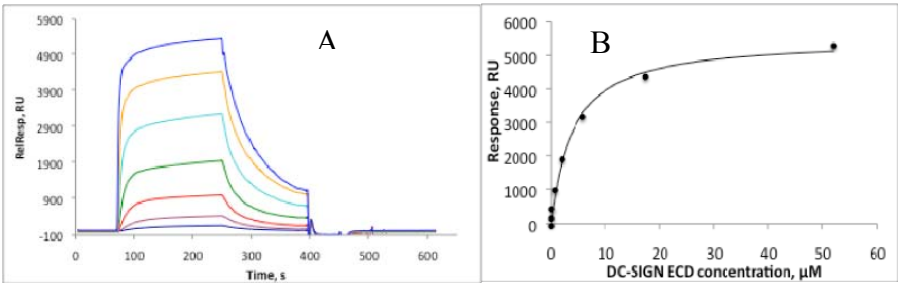


SI-Figure 1. Langerin interaction with reference surface. Data were obtained with 5 µl/min flow rate of running buffer (25 mM Tris-HCl pH 8, 150 mM NaCl, 4 mM $CaCl_2$, 0.005% surfactant P20). Left panel A), reference flow cell corresponds to carboxymethylated dextran surface. Right panel B), reference surface functionalized with unglycosylated BSA.

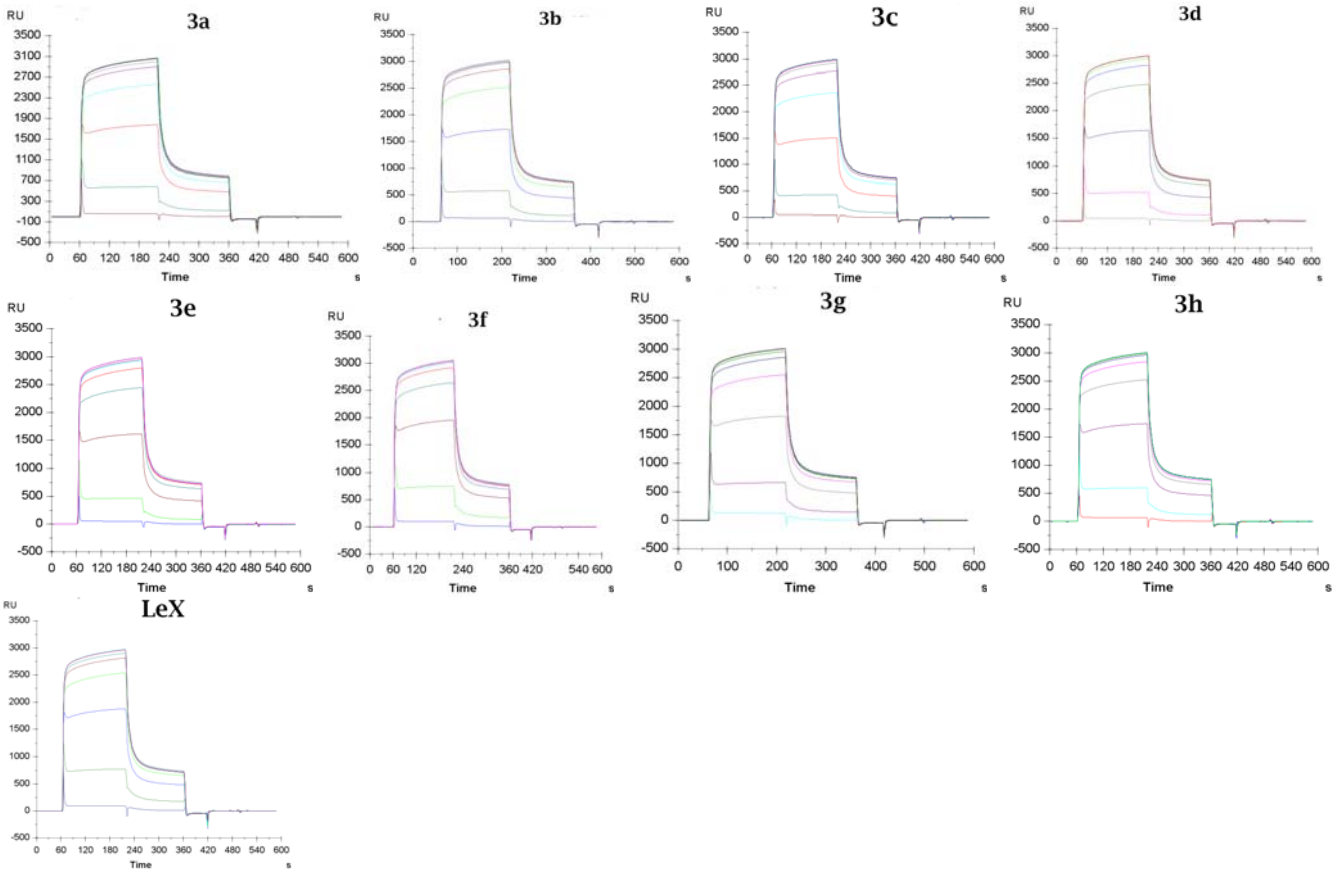


SI-Figure 2: Langerin titration on a Man-BSA surface. A) Langerin concentrations range from 50.35 µM to 0.07 µM by 3-fold dilutions. Regeneration is performed using 1-minute pulse injection of 50 mM EDTA pH 8, at 400 sec. B) Titration curve derived from sensorgrams A).

Supplementary Information

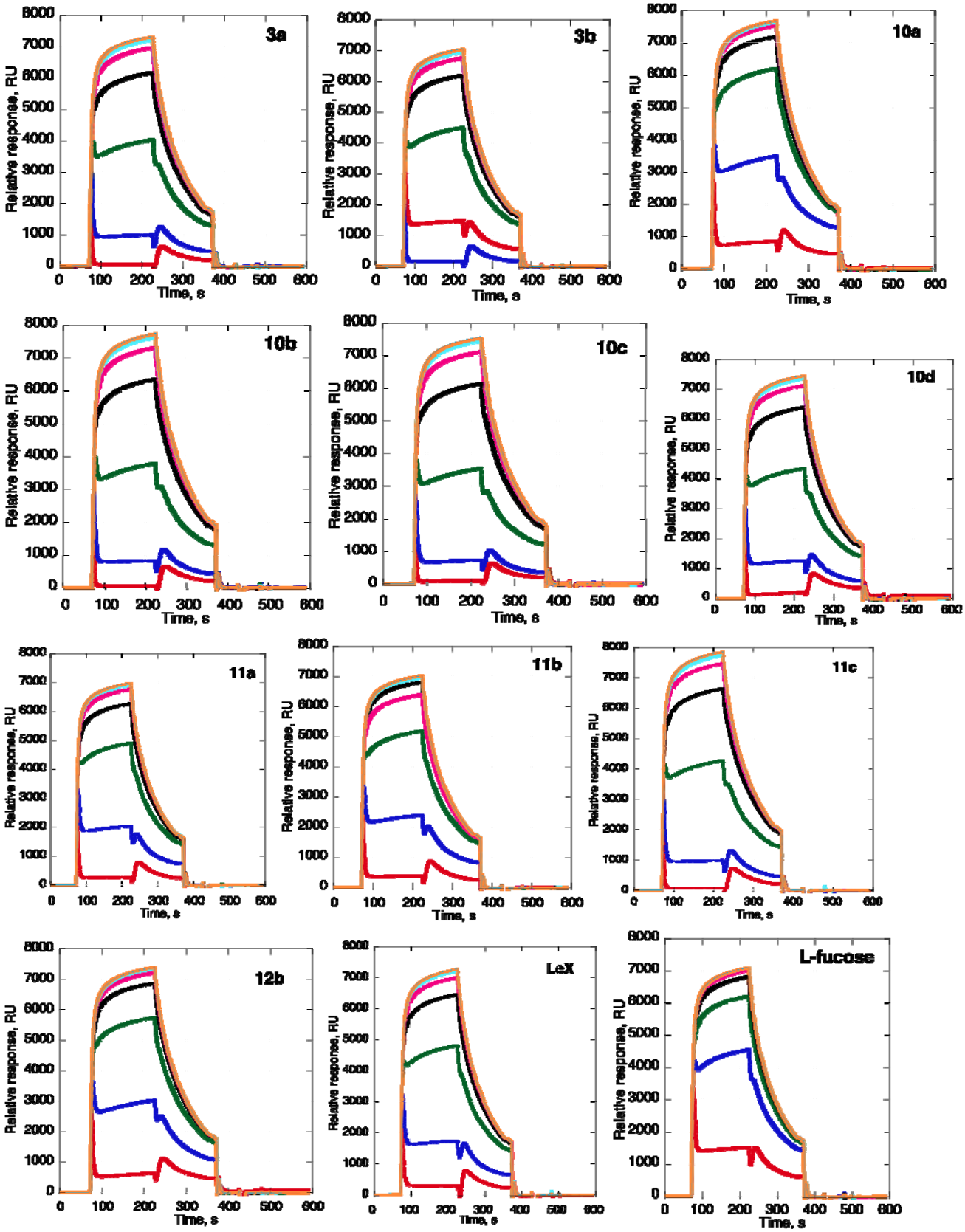


SI-Figure 3: DC-SIGN ECD titration on a Man-BSA surface. A) DC-SIGN ECD concentrations range from 50.35 µM to 0.07 µM by 3-fold dilutions. Regeneration is performed using 1 minute pulse injection of 50 mM EDTA pH 8, at 400 sec. B) Titration curve derived from sensorgrams A).



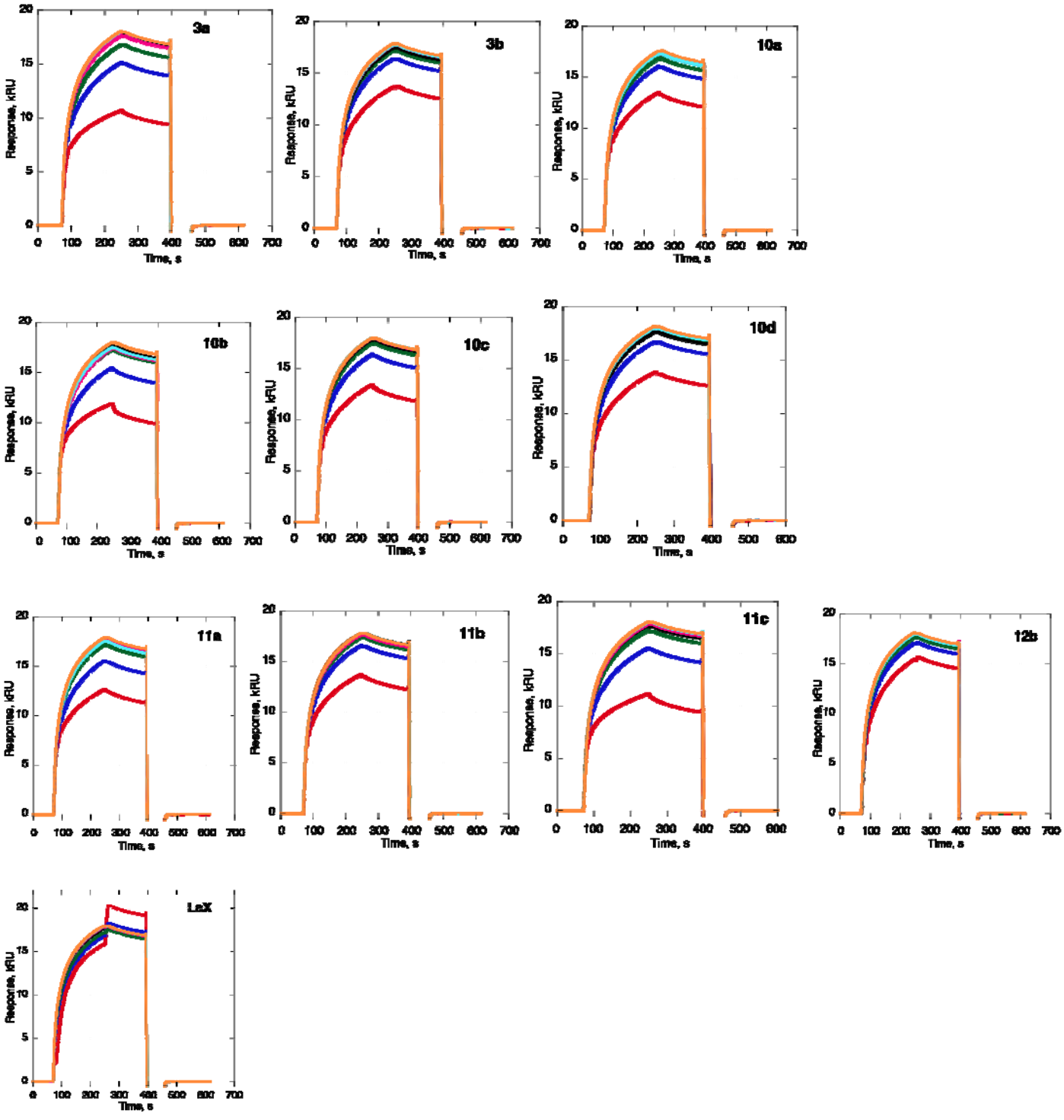
SI-Figure 4: Reference surface corrected overlay sensorgrams representing inhibition of DC-SIGN ECD binding to Man-BSA surface by compounds **3** and LeX.

Supplementary Information



SI-Figure 5: Reference surface corrected overlay sensorgrams representing inhibition of DC-SIGN ECD binding to Man-BSA surface by compounds **3**, **10**, **11**, **12**, L-fucose, and LeX.

Supplementary Information

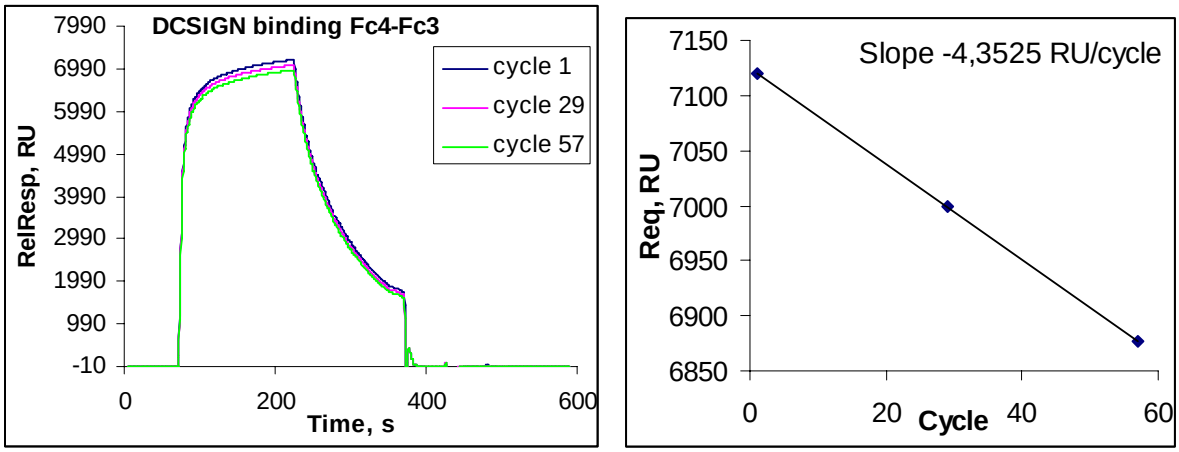


SI-Figure 6: Overlay raw sensorgrams representing inhibition of Langerin ECD binding to Man-BSA/dextran surface by compounds **3**, **10**, **11**, **12**, and LeX.

Supplementary Information

2. Evaluation of BSA-Man SPR surface stability.

The stability of the surface was evaluated in two aspects: affinity and binding capacity. SI- Figure 7a shows the evolution of DC-SIGN binding level onto one of the chips used, plotted as a function of the number of cycles performed onto the chip. The binding level is very reproducible with a deviation of about 4 RU per cycle (Figure 7b) to compare to a binding level close to 7000 RU (so a loss of around 0.06 %).



a. **b.**

SI- Figure 7. a. DC-SIGN binding to BSA-Man chip, as a function of different cycles performed on the chip, b. RU variation as a function of different cycles

Finally, a complete titration of Man-BSA surface with DC-SIGN was performed, to determine apparent Kd, at the beginning and end of each SPR campaign (new surface each time). Very similar values were obtained each time (4.2 µM compared to 3.3 µM; or 6.1 µM compared to 5.5 µM).