Supporting Information for

Combinatorial Solid-Phase Synthesis of Multivalent Cyclic Neoglycopeptides

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Experimental Section

8: Boc-Lys(Aloc)-Orn(Ddv)-Gly-Ala-d-Lys(Ddv)-Orn(Ddv)-d-Val-Glu(OAll)-Bal-Sieber-TG (0.54 g, 70 µmol) was shaken for 16 h under argon with morpholine (77 µl, 0.88 mmol) and Pd(PPh₃)₄ (12 mg, 10 µmol) in DMF/DMSO (1:1) (3 mL) and subsequently washed with DMF and CH₂Cl₂. After treatment of a resin sample with the cleavage cocktail, remaining 8 was extracted with MeOH from the solid support. HPLC (20–80 % acetonitrile in water/0.1 % TFA over 30 min): retention time t_R = 18.5 min; ESI-MS (M + H⁺): calcd. 1648.0, found 1648.6.

9: Boc-Lys-Orn(Ddv)-Gly-Ala-d-Lys(Ddv)-Orn(Ddv)-d-Val-Glu-Bal-Sieber-TG (0.3 g, 38 µmol) was treated for 6 min with a 5 % solution of HOBt in DMF and subsequently washed with DMF. A mixture of HOBt (35 mg, 228 µmol), HBTU (58 mg, 152 µmol), NMP (3 mL), and DIEA (53 µL, 304 µmol) was added and after having been shaken for 11 h at room temperature, the resin was washed with DMF and CH₂Cl₂. HPLC (20–80 % acetonitrile in water/0.1 % TFA over 30 min): t_R = 22.8 min; ESI-MS (M + H⁺): calcd. 1630.0, found 1630.7.

11: cyclo[Boc-Lys-Orn(Ddv)-Gly-Ala-d-Lys(Ddv)-Orn(Ddv)-d-Val-Glu]-Bal-Sieber-TG (0.21 g, 27 µmol) was deprotected by treatment with hydrazine hydrate/DMF (4:96) (5 × 5 min) and washed with DMF. After addition of NMP (2 mL), DIEA (72 µL, 413 µmol), and 5 (240 mg, 413 µmol), the resin was shaken for 6 h at room temperature and subsequently washed with DMF and CH₂Cl₂. Cleavage from the resin was achieved by treatment with
TFA/iPr$_3$SiH/CH$_2$Cl$_2$ (1:1:98) (5 x 5 min, each 4 mL) and thorough washing with F$_3$CCH$_2$OH/CH$_2$Cl$_2$ (1:3) and F$_3$CCH$_2$OH. The combined filtrates were neutralized with pyridine and concentrated under vacuum. Precipitation with tert-butyl methyl ether gave 11 (42 mg, 18 µmol, 67 %). HPLC (20–80 % acetonitrile in water/0.1 % TFA over 30 min): $t_R = 10.6$ min; ESI-MS ($M + H^+$): calcd. 2341.1, found 2342.1.

12: Crude neoglycopeptide 11 (18 mg, 7.7 µmol) was dissolved in CHCl$_3$/MeOH (1:1) (8 mL), a solution of NaOMe in MeOH (5.4 M) (40 µL, 216 µmol) was added, and the mixture was stirred for 3.5 h at room temperature. After neutralization with weakly acidic ion exchange resin (Amberlite IRC-86) the solvent was removed under vacuum. The remaining ion exchange resin was thoroughly washed with water and the combined filtrates were lyophilized to give deacetylated neoglycopeptide 12 (13 mg, 6.6 µmol, 86 %). The content of 12 in the crude product was 95 % (HPLC, 0–50 % acetonitrile in water/0.1 % TFA over 30 min: $t_R = 17.4$ min). Preparative HPLC (10–25 % acetonitrile in water/0.1 % TFA) gave 11 mg of 12.