Electronic Supplementary Information for

Helical peptides from VEGF and Vammin hot-spots for modulating the VEGF/VEGFR interaction

María Isabel García-Aranda,[a] Susana González-López,[a] Clara María Santiveri,[b] Nathalie Gagey-Eilstein,[c] Marie Reille-Seroussi,[c] Mercedes Martín-Martínez,[a] Nicolas Inguimbert,[c,d] Michel Vidal,[c,e] María Teresa García-López,[a] María Angeles Jiménez,[b] Rosario González-Muñiz,[a] María Jesús Pérez de Vega.*[a]

[a]Instituto de Química Médica, CSIC. C/ Juan de la Cierva, 3. 28006 Madrid (Spain).
[b]Instituto de Química-Física Rocasolano, CSIC. C/ Serrano, 119. 28006 Madrid (Spain).
[c]Université Paris Descartes, UFR des Sciences Pharmaceutiques et Biologiques, UMR CNRS 8638, 4 Avenue de l'Observatoire, Paris F-75270 (France).
[d]Université de Perpignan Via Domitia, Laboratoire de Chimie des Biomolécules et de l'Environnement, EA 4215, 52 Avenue P. Alduy, Perpignan F-66860 (France).
[e]UF « Pharmacinétique et Pharmacochimie », GH Cochin – Hôtel Dieu – Broca, Hôpital Cochin, AP-HP, Paris (France).
[f]Departamento de Biología Vascular e Inflamación. Centro Nacional de Investigaciones Cardiovasculares, CNIC. C/ Melchor Fernández Almagro, 3. 28029 Madrid (Spain).

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Synthetic procedures

General: All reagents were of commercial quality. Amino acids and HOBt were provided by NEOMPS, DIC by FLUKA, PyAOP, HOAt, Pd(PPh3)4 and PhSiH3 by ALDRICH and Rink Amide resin by NOVABIOCHEM. Solvents were dried and purified by standard methods. Analytical RP-HPLC was performed on a Waters 600 HPLC equipment equipped with a reverse-phase ACE-5 C18-300 column (4.6 × 250 mm), with a flow rate of 1.3 mL/min, and using a Waters 2487 detector. Mixtures of CH3CN (solvent A) and H2O + 0.05% TFA (solvent B) were used as mobile phase. For purification of all compounds, a semipreparative column ACE 5 C18-300 (10 x 250

mm) was used with the same mixture of solvents than in analytical. Electrospray mass spectra (ES-MS) were performed, in positive mode, in a Waters HPLC-MS ZQ 2000 equipment. HRMS (EI+) was carried out in an Agilent 6520 Accurate-Mass Q-TOF LC/MS equipment.

Resins were swollen in DCM/DMF/DCM/DMF (4 × 0.5 min). All compounds were synthesized manually in parallel on resin, following the Fmoc/*t*Bu strategy, using Fmoc-Glu(OtBu)-OH, Fmoc-Val-OH, Fmoc-Lys(Boc)-OH, Fmoc-Phe-OH, Fmoc-Leu-OH, Fmoc-Ile-OH, Fmoc-Met-OH, Fmoc-Arg(Pbf)-OH, Fmoc-His(Trt)-OH, Fmoc-Asp(OtBu)-OH, Fmoc-Tyr(tBu)-OH, Fmoc-Pro-OH, Fmoc-Gln(Trt)-OH, Fmoc-Ser(tBu)-OH, Fmoc-Asn(Trt)-OH, Fmoc-Ala-OH, Fmoc-Lys(Alloc)-OH or Fmoc-Glu(All)-OH as required, and were isolated in high purity (>98%) by semipreparative HPLC

General coupling procedure. Rink amide resin (100 mg, 0.034 mmol) previously swollen, was treated with 20% piperidine in DMF (1 × 1 min) and (3 × 10 min) and washed with DMF/DCM/DMF/DCM/DMF (4 × 0.5 min). **Method A:** Then a solution of the corresponding amino acid (0.051mmol) in anhydrous DMF (1 ml), HOBt (7.8 mg, 0.051 mmol) and DIC (7.8µl, 0.051 mmol) were added. Couplings were allowed to proceed at room temperature overnight. **Method B:** Then a solution of the corresponding amino acid (0.068 mmol) in anhydrous DMF (1 ml), HCTU (28 mg, 0.068 mmol) and DIEA (22 µl, 0.126 mmol) were added. Couplings were allowed to proceed at room temperature for an hour. When necessary, the coupling was repeated with a fresh portion of Fmoc-amino acid and the indicated coupling reagents. After complete coupling, the resins were drained and washed with DMF/DCM/DMF/DCM (5 × 0.5 min).

Coupling reactions to primary amines were monitored by the Kaiser ninhydrin test and to secondary amines by the cloranil test.

General acetylation procedure. The Fmoc-resin-bounded derivative, previously swollen, was treated with 20% piperidine in DMF (1 × 1 min) and (3 × 10 min) and washed with DMF/DCM/DMF/DCM/DMF (4 × 0.5min). Then a mixture of acetic anhydride/DIEA/DMF (1:1:1) was added (1 × 1 min) and (4 × 10 min) and washed with DMF/DCM/DMF/DCM/DMF (4 × 0.5 min).

General procedure for removing of Alloc and OAll protecting groups: The resin-bounded derivative, previously swollen, was purged with Ar and treated with a solution of $Pd(PPh_3)_4$ (10 mg, 0.008 mmol) and $PhSiH_3$ (0.1 ml, 0.82 mmol) in DCM (2 ml). The reaction mixture is stirred for 45 min. This procedure was repeated once more. The resin was washed with DCM/DMF/Et_2NCS_2Na (0.02M)/DMF/DCM (4 × 0.5 min).

General cleavage procedure. The resin-bounded derivative was treated with 1 ml of TFA/EDT/H_2O/TIS (94:2.5:2.5:1) for 5 h at room temperature. The filtrates were precipitated from diethylether and centrifuged three times at 5000 rpm for 10 min. After the lyophilisation of the compound, the obtained peptide was purified by semipreparative HPLC.

Lactamization reaction. After removing of Alloc and OAll protecting groups, the linear-resin-bounded derivative (100 mg, 0.034 mmol), previously swollen, was treated with a solution of PyAOP (177 mg, 0.34 mmol), HOAt (46 mg, 0.34 mmol), DIEA (0.12 ml, 0.68 mmol) in anhydrous DCE with 15% of trifluoroethanol (2 ml). The reaction was allowed to proceed at 120ºC for 1h under microwave radiation until ninhydrine test was negative. The resin was washed and drained with DMF/DCM/DMF/DCM (4 × 0.5 min).

Characterization of compounds 1-8, 15-18

Ac-Glu^{1}-Val^{2}-Val^{3}-Lys^{4}-Phe^{5}-Met^{6}-Asp^{7}-Val^{8}-Tyr^{9}-Gln^{10}-Arg^{11}-Ser^{12}-Tyr^{13}-NH$_2$ (1): Method A. The peptide was cleaved and purified by semipreparative HPLC (15% A 2 min, 15 to 25% A in 25 min, 25 to 100% A in 3 min) obtaining 4.1 mg of a white solid with a purity of 99% (7% total yield). HPLC: t_R = 22.14 min. ESI-MS: $[M + 2H]^{2+}$ = 853.10. HRMS (EI+) *m/z* 1703.8321 ($[M]^+$ $C_{78}H_{117}N_{19}O_{22}S$, requires 1703.8341).

Ac-Glu^{1}-Val^{2}-Gln^{3}-Lys^{4}-Phe^{5}-Leu^{6}-Glu^{7}-Val^{8}-Tyr^{9}-Leu^{10}-Arg^{11}-Leu^{12}-Tyr^{13}-NH$_2$ (2): Method A. The peptide was cleaved and purified by semipreparative HPLC (20% A 2 min, 20 to 55% A in 25 min, 55 to 100% A en 3 min) obtaining 4.1 mg of a white solid with a purity of 98% (7% total yield). HPLC*:* t_R = 21.64 min. EM-ES: $[M + 2H]^{2+}$ = 871.68, $[M + 3H]^{3+}$ = 581.66. HRMS (EI+) *m/z* 1741.9780 ($[M]^+$ $C_{84}H_{131}N_{19}O_{21}$, requires 1741.9767).

Ac-Ser^{1}-Ser^{2}-Gln^{3}-Lys^{4}-Phe^{5}-Leu^{6}-Glu^{7}-Val^{8}-Tyr^{9}-Gln^{10}-Arg^{11}-Leu^{12}-Tyr^{13}-Asn^{14}-NH$_2$ (3): Method B. The peptide was cleaved and purified by semipreparative HPLC min (10% A 2 min, 10 to 50% A in 25 min, 50 to 100% A in 3 min) obtaining 3.1 mg of a white solid with a purity of 99% (5% total yield). HPLC: t_R = 20.43. EM-ES: $[M + H]^+$ = 1817.6, $[M + 2H]^{2+}$ = 909.3, $[M + 3H]^{3+}$ = 606.5. HRMS (EI+) *m/z* 1814.9302 ($[M]^+$ $C_{83}H_{126}N_{22}O_{24}$, requires 1814.9315).

Ac-Ser^{1}-Ser^{2}-Gln^{3}-Lys^{4}-Phe^{5}-Leu^{6}-Glu^{7}-Val^{8}-Tyr^{9}-Leu^{10}-Arg^{11}-Leu^{12}-Tyr^{13}-Asn^{14}-NH$_2$ (4): Method B. The peptide was cleaved and purified by semipreparative HPLC min (10% A 2 min, 10 to 50% A in 25 min, 50 to 100% A in 3 min) obtaining 4.9 mg of a white solid with a purity of 98% (8% total yield). HPLC: t_R = 22.20 min EM-ES: $[M + H]^+$ = 1802.8, $[M + 2H]^{2+}$ = 901.3. HRMS (EI+) *m/z* 1799.9615 ($[M]^+$ $C_{84}H_{129}N_{21}O_{23}$, requires 1799.9570).

Ac-Glu^{1}-Val^{2}-Arg^{3}-Pro^{4}-Phe^{5}-Leu^{6}-Glu^{7}-Val^{8}-His^{9}-Glu^{10}-Arg^{11}-Ser^{12}-Ala^{13}-NH$_2$ (5): Method B. The peptide was cleaved and purified by semipreparative HPLC (15% A 2 min, 15 to 30% A in 25 min, 30 to 100% A in 3 min) obtaining 4.4 mg of a white solid with a purity of 99% (8% total yield). HPLC: t_R = 18.42 min. EM-ES: $[M + H]^+$ = 1610.6, $[M + 2H]^{2+}$ = 806.0, $[M + 3H]^{3+}$ = 537.7. HRMS (EI+) *m/z* 1607.8448 ($[M]^+$ $C_{72}H_{113}N_{21}O_{21}$, requires 1607.8420).

Ac-Asp^{1}-Val^{2}-Arg^{3}-Arg^{4}-Phe^{5}-Leu^{6}-Glu^{7}-Val^{8}-His^{9}-Leu^{10}-Arg^{11}-Leu^{12}-Ala^{13}-NH$_2$ (6): Method A. The peptide was cleaved and purified by semipreparative HPLC (15% A 2 min, 15 to 55% A in 25 min, 55 to 100% A in 3 min) obtaining 2.3 mg of a white solid with a purity of 98% (4% total yield). HPLC*:* t_R = 18.02 min EM-ES: $[M + 2H]^{2+}$ = 834.17, $[M + 3H]^{3+}$ = 556.39, $[M + 4H]^{4+}$ = 417.63. HRMS (EI+) *m/z* 1663.9631 ($[M]^+$ $C_{75}H_{125}N_{25}O_{18}$, requires 1663.9634).

Ac-Asp^{1}-Leu^{2}-Arg^{3}-Ala^{4}-Phe^{5}-Leu^{6}-Glu^{7}-Gln^{8}-His^{9}-Leu^{10}-Arg^{11}-Ser^{12}-Ala^{13}-NH$_2$ (7): Method B. The peptide was cleaved and purified by semipreparative HPLC (10% A 2 min, 10 to 50% A in 25 min, 50 to 100% A in 3 min) obtaining 4.3 mg of a white

solid with a purity of 98% (8% total yield). HPLC: t_R = 21.33 min EM-ES: $[M + H]^+$ = 1597.3, $[M + 2H]^{2+}$ = 799.3, $[M + 3H]^{3+}$ = 533.3. HRMS (EI+) *m/z* 1595.8508 ($[M]^+$ $C_{70}H_{113}N_{23}O_{20}$, requires 1595.8532).

Ac-Ser^1-Val^2-Arg^3-Arg^4-Phe^5-Leu^6-Glu^7-Ala^8-His^9-Leu^{10}-Arg^{11}-Leu^{12}-Ala^{13}-NH$_2$ (8): Method B. The peptide was cleaved and purified by semipreparative HPLC (10% A 2 min, 10 to 50% A in 25 min, 50 to 100% A in 3 min) obtaining 4.9 mg of a white solid with a purity of 98% (9% total yield). HPLC: t_R = 21.02 min. EM-ES $[M + 2H]^{2+}$ = 805.3, $[M + 3H]^{3+}$ = 537.3. HRMS (EI+) *m/z* 1607.9374 ($[M]^+$ $C_{72}H_{121}N_{25}O_{17}$, requires 1607.9372).

Ac-Glu^1-Val^2-Glu^3-Lys^4-Phe^5-Met(O$_2$)^6-Lys^7-Val^8-Tyr^9-Gln^{10}-Arg^{11}-Ser^{12}-Tyr^{13}-NH$_2$ (15): After the elongation of the peptide, using Method B, the Alloc and OAll groups were removed from the resin-bounded derivative. Then the peptide was cleaved and purified by semipreparative HPLC (15% A 2 min, 15 to 25% A in 25 min, 25 to 100% A in 3 min) obtaining 1.2 mg of a white solid with a purity of 99% (2% total yield). HPLC: t_R = 23.74 min. EM-ES: $[M + H]^+$ = 1780.6, $[M + 2H]^{2+}$ = 890.8, $[M + 3H]^{3+}$ = 594.3. HRMS (EI+) m/z 1778.8666 ($[M]^+$ $C_{80}H_{122}N_{20}O_{24}S$, requires 1778.8662).

Ac-Glu^1-Val^2-*c*(NH-CO)$^{3\text{-}7}$[Glu^3-Lys^4-Phe^5-Met(O$_2$)^6-Lys^7]-Val^8-Tyr^9-Gln^{10}-Arg^{11}-Ser^{12}-Tyr^{13}-NH$_2$ (16): Over the compound 11 anchored to the resin, lactamization reaction was allowed to proceed under microwave radiation. After the cleavage, this peptide was purified by semipreparative HPLC (15% A 2 min, 15 to 45% A in 25 min, 45 to 100% A in 3 min) yielding 0.6 mg of a white solid with a purity of 99% (1% total yield). HPLC: t_R = 19.30 min. EM-ES: $[M + H]^+$ = 1763.3, $[M + 2H]^{2+}$ = 881.7. HRMS (EI+) m/z 1760.8536 ($[M]^+$ $C_{80}H_{120}N_{20}O_{23}S$, requires 1760.8556).

Ac-Glu^1-Val^2-Val^3-Lys^4-Phe^5-Met(O$_2$)^6-Glu^7-Val^8-Tyr^9-Gln^{10}-Lys^{11}-Ser^{12}-Tyr^{13}-NH$_2$ (17): After the elongation of the peptide, using Method B, the Alloc and OAll groups were removed from the resin-bounded derivative. Then the peptide was cleaved and purified by semipreparative HPLC (15% A 2 min, 15 to 45% A in 25 min, 45 to 100% A in 3 min) obtaining 2.9 mg of a white solid with a purity of 99% (5% total yield). HPLC: t_R = 17.64 min. EM-ES: $[M + H]^+$ = 1724.6, $[M + 2H]^{2+}$ = 862.8. HRMS (EI+) m/z 1721.8350 ($[M]^+$ $C_{79}H_{119}N_{17}O_{24}S$, requires 1721.8335).

Ac-Glu^1-Val^2-Val^3-Lys^4-Phe^5-Met(O$_2$)^6-*c*(NH-CO)$^{7\text{-}11}$[Glu^7-Val^8-Tyr^9-Gln^{10}-Lys^{11}]-Ser^{12}-Tyr^{13}-NH$_2$ (18): Over the compound 13 anchored to the resin, lactamization reaction was allowed to proceed under microwave radiation. After the cleavage, this peptide was purified by semipreparative HPLC (15% A 2 min, 15 to 55% A in 25 min, 55 to 100% A in 3 min) yielding 1.2 mg of a white solid with a purity of 99% (2% total yield). HPLC: t_R = 18.08 min. EM-ES: $[M + H]^+$ = 1705.6, $[M + 2H]^{2+}$ = 853.3, $[M + 3H]^{3+}$ = 543.5. HRMS (EI+) m/z 1703.8227 ($[M]^+$ $C_{79}H_{117}N_{17}O_{23}S$, requires 1703.8229).

Table ST1. ^{1}H, and ^{13}C chemical shifts (ppm, from DSS) for compound **1** in 30%TFE at 25ºC.

Ac-Glu^{1}-Val^{2}-Val^{3}-Lys^{4}-Phe^{5}-Met^{6}-Asp^{7}-Val^{8}-Tyr^{9}-Gln^{10}-Arg^{11}-Ser^{12}-Tyr^{13}-NH$_2$

Residue	HN	$^{13}C_\alpha$	$C_\alpha H$	$^{13}C_\beta$	$C_\beta H$	Others
CH_3CO						CH_3 2.10; ^{13}C 24.5
Glu 1	8.39	58.3	4.22	30.1	2.00, 2.10	$C_{\gamma\gamma'}H$ 2.36, 2.36; $^{13}C_\gamma$ 36.5
Val 2	7.96	64.7	3.99	32.5	2.13	$C_\gamma H_3$ 0.99; $^{13}C_\gamma$ 20.7
						$C_{\gamma'}H_3$ 1.04; $^{13}C_{\gamma'}$ 21.1
Val 3	7.56	65.0	3.90	32.2	2.14	$C_\gamma H_3$ 0.98; $^{13}C_\gamma$ 21.1
						$C_{\gamma'}H_3$ 1.02; $^{13}C_{\gamma'}$ 21.3
Lys 4	7.79	58.3	4.22	32.7	1.86, 1.86	$C_{\gamma\gamma'}H$ 1.40, 1.46; $^{13}C_\gamma$ 25.2
						$C_{\delta\delta'}H$ 1.71, 1.71; $^{13}C_\delta$ 29.5
						$C_{\varepsilon\varepsilon'}H$ 2.96, 2.96; $^{13}C_\varepsilon$ 42.4
Phe 5	8.04	60.5	4.39	39.2	3.20, 3.20	$C_{\delta\delta'}H$ 7.22, 7.22
						$C_{\varepsilon\varepsilon'}H$ 7.26, 7.26
						$C_\zeta H$ ----
Met 6	8.31	60.3	4.31	32.4	2.15, 2.22	$C_{\gamma\gamma'}H$ 2.64, 2.76; $^{13}C_\gamma$ 32.6
						$C_\varepsilon H_3$ 2.08; $^{13}C_\varepsilon$ 16.5
Asp 7	8.07	nd	4.53	41.7	2.84, 2.84	
Val 8	7.78	66.0	3.70	32.3	2.14	$C_\gamma H_3$ 0.88; $^{13}C_\gamma$ 20.9
						$C_{\gamma'}H_3$ 1.01; $^{13}C_{\gamma'}$ 21.8
Tyr 9	8.48	61.6	4.15	38.7	2.84, 3.07	$C_{\delta\delta'}H$ 7.06, 7.06
						$C_{\varepsilon\varepsilon'}H$ 6.77, 6.77
Gln 10	8.40	58.6	4.07	29.0	2.22, 2.26	$C_{\gamma\gamma'}H$ 2.48, 2.62; $^{13}C_\gamma$ 34.6
						$N_{\varepsilon\varepsilon'}H_2$ 6.70, 7.26
Arg 11	7.95	58.1	4.19	30.7	1.87, 1.87	$C_{\gamma\gamma'}H$ 1.68, 1.82; $^{13}C_\gamma$ 28.1
						$C_{\delta\delta'}H$ 3.14, 3.21; $^{13}C_\delta$ 43.7
						$N_\varepsilon H$ 7.40
Ser 12	7.88	60.3	4.31	64.0	3.58, 3.72	
Tyr 13	7.87	nd	4.45	39.2	2.61, 3.03	$C_{\delta\delta'}H$ 7.00, 7.00
						$C_{\varepsilon\varepsilon'}H$ 6.77, 6.77
$CONH_2$	6.96, 7.26					

Table ST2. ^{1}H, and ^{13}C chemical shifts (ppm, from DSS) for compound **2** in 30%TFE at 25ºC.

Ac-Glu^{1}-Val^{2}-Gln^{3}-Lys^{4}-Phe^{5}-Leu^{6}-Glu^{7}-Val^{8}-Tyr^{9}-Leu^{10}-Arg^{11}-Leu^{12}-Tyr^{13}-NH$_2$

Residue	HN	$^{13}C_\alpha$	$C_\alpha H$	$^{13}C_\beta$	$C_\beta H$	Others
CH_3CO						CH_3 2.12; ^{13}C 24.6
Glu 1	8.36	58.3	4.26	29.8	2.03, 2.14	$C_{\gamma\gamma'}H$ 2.36, 2.36; $^{13}C_\gamma$ 36.5
Val 2	8.07	65.9	3.88	32.1	2.10	$C_\gamma H_3$ 0.99; $^{13}C_\gamma$ 20.6
						$C_{\gamma'}H_3$ 1.06; $^{13}C_{\gamma'}$ 21.6
Gln 3	8.32	59.9	4.01	28.2	2.11, 2.15	$C_{\gamma\gamma'}H$ 2.44, 2.47; $^{13}C_\gamma$ 34.4
						$N_{\varepsilon\varepsilon'}H_2$ 6.70, 7.42
Lys 4	7.72	59.1	4.14	32.3	1.91, 1.91	$C_{\gamma\gamma'}H$ 1.40, 1.46; $^{13}C_\gamma$ nd
						$C_{\delta\delta'}H$ 1.71, 1.71; $^{13}C_\delta$ 29.2
						$C_{\varepsilon\varepsilon'}H$ 2.96, 2.96; $^{13}C_\varepsilon$ 42.4
Phe 5	7.81	nd	4.34	39.1	3.23, 3.27	$C_{\delta\delta'}H$ 7.14, 7.14
						$C_{\varepsilon\varepsilon'}H$ 7.21, 7.21
						$C_\zeta H$ ----
Leu 6	8.34	58.4	4.04	42.1	1.63, 1.87	$C_\gamma H$ 1.88; $^{13}C_\gamma$ 27.2
						$C_\delta H_3$ 0.90; $^{13}C_\delta$ 23.1
						$C_{\delta'}H_3$ 0.92; $^{13}C_{\delta'}$ 25.1
Glu 7	7.98	60.1	3.95	29.4	2.14, 2.25	$C_{\gamma\gamma'}H$ 2.33, 2.55; $^{13}C_\gamma$ 36.0
Val 8	7.59	66.8	3.64	32.2	2.19	$C_\gamma H_3$ 0.93; $^{13}C_\gamma$ 21.1
						$C_{\gamma'}H_3$ 1.08; $^{13}C_{\gamma'}$ 22.3
Tyr 9	8.45	nd	3.98	39.0	2.77, 3.01	$C_{\delta\delta'}H$ 6.96, 6.96
						$C_{\varepsilon\varepsilon'}H$ 6.67, 6.67
Leu 10	8.73	57.9	4.02	42.0	1.49, 1.95	$C_\gamma H$ 2.00; $^{13}C_\gamma$ 27.4
						$C_\delta H_3$ 0.93; $^{13}C_\delta$ 22.4
						$C_{\delta'}H_3$ 0.96; $^{13}C_{\delta'}$ 24.5
Arg 11	7.69	58.8	4.08	30.3	1.91, 1.99	$C_{\gamma\gamma'}H$ 1.67, 1.84; $^{13}C_\gamma$ 28.0
						$C_{\delta\delta'}H$ 3.18, 3.18; $^{13}C_\delta$ 43.5
						$N_\varepsilon H$ 7.36
Leu 12	8.02	57.2	4.07	43.1	0.87, 1.44	$C_\gamma H$ 1.55; $^{13}C_\gamma$ 26.9
						$C_\delta H_3$ 0.70; $^{13}C_\delta$ 22.6
						$C_{\delta'}H_3$ 0.76; $^{13}C_{\delta'}$ 24.9
Tyr 13	8.16	nd	4.44	39.2	2.31, 2.97	$C_{\delta\delta'}H$ 6.90, 6.90
						$C_{\varepsilon\varepsilon'}H$ 6.72, 6.72
$CONH_2$	6.84, 7.21					

Table ST3. ^{1}H, and ^{13}C chemical shifts (ppm, from DSS) for compound **3** in 30%TFE at 25ºC.

Ac-Ser^{1}-Ser^{2}-Gln^{3}-Lys^{4}-Phe^{5}-Leu^{6}-Glu^{7}-Val^{8}-Tyr^{9}-Gln^{10}-Arg^{11}-Leu^{12}-Tyr^{13}-Asn^{14}-NH_2

Residue	HN	$^{13}C_\alpha$	$C_\alpha H$	$^{13}C_\beta$	$C_\beta H$	Others
CH_3CO						CH_3 2.10; ^{13}C 24.6
Ser 1	8.06	59.0	4.48	64.2	3.90, 4.01	
Ser 2	8.47	60.2	4.44	63.5	3.97, 402	
Gln 3	8.34	58.7	4.18	28.7	2.12, 2.12	$C_{\gamma\gamma'}H$ 2.44, 2.44; $^{13}C_\gamma$ 34.1 $N_{\varepsilon\varepsilon'}H_2$ 6.73, 7.42
Lys 4	7.95	58.7	4.17	32.2	1.86, 1.86	$C_{\gamma\gamma'}H$ 1.46, 1.46; $^{13}C_\gamma$ 24.9 $C_{\delta\delta'}H$ 1.71, 1.71; $^{13}C_\delta$ 29.0 $C_{\varepsilon\varepsilon'}H$ 2.96, 2.96; $^{13}C_\varepsilon$ 42.3
Phe 5	7.89	61.0	4.32	39.0	3.20, 3.20	$C_{\delta\delta'}H$ 7.27, 7.27 $C_{\varepsilon\varepsilon'}H$ 7.22, 7.22 $C_\zeta H$ ----
Leu 6	7.89	58.2	4.10	42.0	1.67, 1.86	$C_\gamma H$ 1.79; $^{13}C_\gamma$ 27.3 $C_\delta H_3$ 0.92; $^{13}C_\delta$ 23.3 $C_{\delta'}H_3$ 0.97; $^{13}C_{\delta'}$ 24.6
Glu 7	7.95	59.6	4.09	29.3	2.17, 2.26	$C_{\gamma\gamma'}H$ 2.37, 2.54; $^{13}C_\gamma$ 35.5
Val 8	7.79	66.7	3.65	32.1	2.16	$C_\gamma H_3$ 0.91; $^{13}C_\gamma$ 20.8 $C_{\gamma'}H_3$ 1.05; $^{13}C_{\gamma'}$ 22.1
Tyr 9	8.38	62.0	4.06	38.6	2.85, 3.02	$C_{\delta\delta'}H$ 7.00, 7.00 $C_{\varepsilon\varepsilon'}H$ 6.71, 6.71
Gln10	8.30	59.2	3.99	29.1	2.18, 2.27	$C_{\gamma\gamma'}H$ 2.44, 2.461; $^{13}C_\gamma$ 34.6 $N_{\varepsilon\varepsilon'}H_2$ 6.68, 7.07
Arg 11	7.80	58.6	4.16	30.2	1.97, 1.97	$C_{\gamma\gamma'}H$ 1.72, 1.83; $^{13}C_\gamma$ 27.7 $C_{\delta\delta'}H$ 3.21, 3.21; $^{13}C_\delta$ 43.4 $N_\varepsilon H$ 7.33
Leu 12	8.13	57.1	4.13	42.6	1.20, 1.54	$C_\gamma H$ 1.64; $^{13}C_\gamma$ 26.9 $C_\delta H_3$ 0.78; $^{13}C_\delta$ 22.6 $C_{\delta'}H_3$ 0.82; $^{13}C_{\delta'}$ 24.9
Tyr 13	8.09	59.6	4.36	38.7	2.61, 2.93	$C_{\delta\delta'}H$ 6.99, 6.99 $C_{\varepsilon\varepsilon'}H$ 6.78, 6.78
Asn 14	7.81	nd	4.68	39.5	2.78, 2.89	$N_{\delta\delta'}H_2$ 6.77, 7.58
$CONH_2$	6.93, 7.10					

Table ST4. ^{1}H, and ^{13}C chemical shifts (ppm, from DSS) for compound **4** in 30%TFE at 25ºC.

Ac-Ser^{1}-Ser^{2}-Gln^{3}-Lys^{4}-Phe^{5}-Leu^{6}-Glu^{7}-Val^{8}-Tyr^{9}-Leu^{10}-Arg^{11}-Leu^{12}-Tyr^{13}-Asn^{14}-NH_2

Residue	HN	$^{13}C_\alpha$	$C_\alpha H$	$^{13}C_\beta$	$C_\beta H$	Others
CH_3CO						CH_3 2.10; ^{13}C 24.6
Ser 1	8.03	59.0	4.49	64.2	3.90, 4.02	
Ser 2	8.46	60.4	4.44	63.5	3.98, 402	
Gln 3	8.35	58.9	4.18	28.7	2.13, 2.13	$C_{\gamma\gamma'}H$ 2.45, 2.45; $^{13}C_\gamma$ 34.2 $N_{\varepsilon\varepsilon'}H_2$ 6.70, 7.40
Lys 4	7.95	58.8	4.17	32.2	1.86, 1.86	$C_{\gamma\gamma'}H$ 1.46, 1.46; $^{13}C_\gamma$ nd $C_{\delta\delta'}H$ 1.71, 1.71; $^{13}C_\delta$ 29.0 $C_{\varepsilon\varepsilon'}H$ 2.96, 2.96; $^{13}C_\varepsilon$ 42.4
Phe 5	7.89	60.9	4.35	39.0	3.20, 3.20	$C_{\delta\delta'}H$ 7.23, 7.23 $C_{\varepsilon\varepsilon'}H$ 7.22, 7.22 $C_\zeta H$ ----
Leu 6	7.89	58.4	4.11	42.2	1.78, 1.78	$C_\gamma H$ 1.79; $^{13}C_\gamma$ 27.3 $C_\delta H_3$ 0.95; $^{13}C_\delta$ 23.8 $C_{\delta'}H_3$ 0.99; $^{13}C_{\delta'}$ 24.0
Glu 7	7.95	60.1	3.96	29.3	2.16, 2.26	$C_{\gamma\gamma'}H$ 2.36, 2.53; $^{13}C_\gamma$ 35.6
Val 8	7.79	66.8	3.64	32.2	2.18	$C_\gamma H_3$ 0.93; $^{13}C_\gamma$ 20.9 $C_{\gamma'}H_3$ 1.07; $^{13}C_{\gamma'}$ 22.3
Tyr 9	8.38	nd	4.06	38.7	2.88, 3.06	$C_{\delta\delta'}H$ 7.00, 7.00 $C_{\varepsilon\varepsilon'}H$ 6.70, 6.70
Leu10	8.30	58.1	4.04	42.1	1.50, 1.98	$C_\gamma H$ 2.00; $^{13}C_\gamma$ 27.3 $C_\delta H_3$ 0.94; $^{13}C_\delta$ 22.5 $C_{\delta'}H_3$ 0.94; $^{13}C_{\delta'}$ 25.2
Arg 11	7.80	58.9	4.13	30.1	1.95, 2.02	$C_{\gamma\gamma'}H$ 1.71, 1.86; $^{13}C_\gamma$ 28.0 $C_{\delta\delta'}H$ 3.20, 3.20; $^{13}C_\delta$ 43.5 $N_\varepsilon H$ 7.35
Leu 12	8.13	57.2	4.15	42.5	1.26, 1.70	$C_\gamma H$ 1.70; $^{13}C_\gamma$ 26.9 $C_\delta H_3$ 0.80; $^{13}C_\delta$ 22.7 $C_{\delta'}H_3$ 0.84; $^{13}C_{\delta'}$ 24.9
Tyr 13	8.09	59.9	4.30	38.9	2.67, 2.93	$C_{\delta\delta'}H$ 7.03, 7.03 $C_{\varepsilon\varepsilon'}H$ 6.82, 6.82
Asn 14	7.81	nd	4.64	39.7	2.76, 2.86	$N_{\delta\delta'}H_2$ 6.66, 7.54
$CONH_2$	6.93, 7.10					

Table ST5. ^{1}H, and ^{13}C chemical shifts (ppm, from DSS) for compound **5** in 30%TFE at 25ºC.

Ac-Glu^{1}-Val^{2}-Arg^{3}-Pro^{4}-Phe^{5}-Leu^{6}-Glu^{7}-Val^{8}-His^{9}-Glu^{10}-Arg^{11}-Ser^{12}-Ala^{13}-NH$_2$

Residue	HN	$^{13}C_\alpha$	$C_\alpha H$	$^{13}C_\beta$	$C_\beta H$	Others
CH_3CO						CH_3 2.10; ^{13}C 24.4
Glu 1	8.24	57.0	4.34	30.6	1.98, 2.07	$C_{\gamma\gamma'}H$ 2.36, 2.36; $^{13}C_\gamma$ 36.5
Val 2	7.92	62.6	4.27	33.1	2.21	$C_\gamma H_3$ 0.97; $^{13}C_\gamma$ 20.1
						$C_{\gamma'}H_3$ 0.99; $^{13}C_{\gamma'}$ 21.0
Arg 3	8.28	57.5	4.45	29.5	1.86, 1.86	$C_{\gamma\gamma'}H$ 1.70, 1.74; $^{13}C_\gamma$ 27.5
						$C_{\delta\delta'}H$ 3.23, 3.23; $^{13}C_\delta$ 43.6[a]
						$N_\varepsilon H$ 7.56
Pro 4		65.1	4.37	31.5	1.75, 2.25	$C_{\gamma\gamma'}H$ 1.99, 1.99; $^{13}C_\gamma$ 27.8
						$C_{\delta\delta'}H$ 3.63, 3.71; $^{13}C_\delta$ 50.5
Phe 5	7.57	59.5	4.45	39.2	3.22, 3.22	$C_{\delta\delta'}H$ 7.25, 7.25
						$C_{\varepsilon\varepsilon'}H$ 7.34, 7.34
						$C_\zeta H$ ----
Leu 6	7.96	57.1	4.22	42.4	1.63, 1.81	$C_\gamma H$ 1.72; $^{13}C_\gamma$ 27.2
						$C_\delta H_3$ 0.92; $^{13}C_\delta$ 23.0
						$C_{\delta'}H_3$ 0.96; $^{13}C_{\delta'}$ 24.9
Glu 7	8.27	58.6	4.18	30.1	2.08, 2.08	$C_{\gamma\gamma'}H$ 2.28, 2.38; $^{13}C_\gamma$ 36.4
Val 8	7.86	64.8	3.88	32.4	2.12	$C_\gamma H_3$ 0.90; $^{13}C_\gamma$ 20.9
						$C_{\gamma'}H_3$ 1.00; $^{13}C_{\gamma'}$ 21.4
His 9	8.24	58.1	4.45	29.1	3.15, 3.30	$C_{\delta 1}H$ 7.23
						$C_{\varepsilon 2}H$ 8.33
Glu 10	8.45	58.2	4.22	30.1	2.14, 2.14	$C_{\gamma\gamma'}H$ 2.38, 2.38; $^{13}C_\gamma$ 36.0
Arg 11	8.22	57.5	4.31	30.8	1.89, 1.96	$C_{\gamma\gamma'}H$ 1.73, 1.79; $^{13}C_\gamma$ 27.6
						$C_{\delta\delta'}H$ 3.22, 3.22; $^{13}C_\delta$ 43.6[a]
						$N_\varepsilon H$ 7.38
Ser 12	8.06	59.3	4.43	64.4	3.91, 3.96	
Ala13	7.98	52.8	4.31	19.5	1.42	
$CONH_2$	6.94, 7.34					

Table ST6. ^{1}H, and ^{13}C chemical shifts (ppm, from DSS) for compound **6** in 30%TFE at 25ºC.

Ac-Asp^{1}-Val^{2}-Arg^{3}-Arg^{4}-Phe^{5}-Leu^{6}-Glu^{7}-Val^{8}-His^{9}-Leu^{10}-Arg^{11}-Leu^{12}-Ala^{13}-NH$_2$

Residue	HN	$^{13}C_\alpha$	$C_\alpha H$	$^{13}C_\beta$	$C_\beta H$	Others
CH_3CO						CH_3 2.05; ^{13}C 24.5
Asp 1	7.90	nd	nd	41.4	2.65, 2.90	
Val 2	8.15	65.5	3.90	32.3	2.17	$C_\gamma H_3$ 1.03; $^{13}C_\gamma$ 20.5 $C_{\gamma'} H_3$ 1.06; $^{13}C_{\gamma'}$ 22.4
Arg 3	8.16	60.1	4.04	30.0	1.98, 1.98	$C_{\gamma\gamma'}H$ 1.71, 1.79; $^{13}C_\gamma$ 27.6 $C_{\delta\delta'}H$ 3.26, 3.26; $^{13}C_\delta$ 43.5[a] $N_\varepsilon H$ 7.70
Arg 4	7.80	59.1	4.17	30.1	1.92, 1.92	$C_{\gamma\gamma'}H$ 1.71, 1.71; $^{13}C_\gamma$ 27.5 $C_{\delta\delta'}H$ 3.25, 3.25; $^{13}C_\delta$ 43.5[a] $N_\varepsilon H$ 7.30
Phe 5	7.91	61.6	4.30	39.3	3.23, 3.38	$C_{\delta\delta'}H$ 7.14, 7.14 $C_{\varepsilon\varepsilon'}H$ 7.22, 7.22 $C_\zeta H$ ----
Leu 6	8.65	58.8	4.10	42.1	1.68, 2.00	$C_\gamma H$ 1.96; $^{13}C_\gamma$ 27.2 $C_\delta H_3$ 0.95; $^{13}C_\delta$ 22.9 $C_{\delta'} H_3$ 0.96; $^{13}C_{\delta'}$ 24.5
Glu 7	8.38	60.6	3.95	29.7	2.16, 2.28	$C_{\gamma\gamma'}H$ 2.30, 2.52; $^{13}C_\gamma$ 36.4
Val 8	8.09	66.8	3.65	32.2	2.09	$C_\gamma H_3$ 0.79; $^{13}C_\gamma$ 20.7 $C_{\gamma'} H_3$ 1.07; $^{13}C_{\gamma'}$ 21.1
His 9	7.87	60.8	4.08	28.2	3.02, 3.21	$C_{\delta 1}H$ 6.99 $C_{\varepsilon 2}H$ 7.83
Leu 10	8.61	58.0	4.15	42.0	1.55, 1.93	$C_\gamma H$ 1.83; $^{13}C_\gamma$ 27.2 $C_\delta H_3$ 0.90; $^{13}C_\delta$ 22.7 $C_{\delta'} H_3$ 0.91; $^{13}C_{\delta'}$ 24.9
Arg 11	7.96	58.8	4.13	30.1	1.95, 1.95	$C_{\gamma\gamma'}H$ 1.71, 1.86; $^{13}C_\gamma$ 28.0 $C_{\delta\delta'}H$ 3.18, 3.18; $^{13}C_\delta$ 43.4 $N_\varepsilon H$ 7.48
Leu 12	7.94	56.7	4.24	42.5	1.53, 1.78	$C_\gamma H$ 1.80; $^{13}C_\gamma$ 27.0 $C_\delta H_3$ 0.79; $^{13}C_\delta$ 22.5 $C_{\delta'} H_3$ 0.84; $^{13}C_{\delta'}$ 25.1
Ala13	7.80	53.2	4.22	19.1	1.43	
$CONH_2$	6.91, 7.13					

Table ST7. ^{1}H, and ^{13}C chemical shifts (ppm, from DSS) for compound **7** in 30%TFE at 25ºC.

Ac-Asp[1]-Leu[2]-Arg[3]-Ala[4]-Phe[5]-Leu[6]-Glu[7]-Gln[8]-His[9]-Leu[10]-Arg[11]-Ser[12]-Ala[13]-NH_2

Residue	HN	$^{13}C_\alpha$	$C_\alpha H$	$^{13}C_\beta$	$C_\beta H$	Others
CH_3CO						CH_3 2.04; ^{13}C 24.6
Asp 1	7.82	nd	4.69	41.8	2.68, 2.88	
Leu 2	8.20	57.9	4.24	42.5	1.66, 1.77	$C_\gamma H$ 1.73; $^{13}C_\gamma$ 27.3 $C_\delta H_3$ 0.90; $^{13}C_\delta$ 23.4 $C_{\delta'} H_3$ 0.97; $^{13}C_{\delta'}$ 24.3
Arg 3	8.14	60.4	3.97	29.8	1.98, 1.98	$C_{\gamma\gamma'} H$ 1.68, 1.77; $^{13}C_\gamma$ 27.4 $C_{\delta\delta'} H$ 3.25, 3.25; $^{13}C_\delta$ 43.6 $N_\varepsilon H$ 7.66
Ala 4	7.87	55.3	4.19	18.2	1.51	
Phe 5	8.01	61.6	4.33	39.4	3.27, 3.38	$C_{\delta\delta'} H$ 7.23, 7.23 $C_{\varepsilon\varepsilon'} H$ 7.14, 7.14 $C_\zeta H$ ----
Leu 6	8.85	58.9	4.05	41.9	1.63, 2.01	$C_\gamma H$ 1.97; $^{13}C_\gamma$ 27.2 $C_\delta H_3$ 0.95; $^{13}C_\delta$ 22.7 $C_{\delta'} H_3$ 0.96; $^{13}C_{\delta'}$ 24.6
Glu 7	8.66	60.4	3.95	29.5	2.12, 2.22	$C_{\gamma\gamma'} H$ 2.29, 2.53; $^{13}C_\gamma$ 36.5
Gln 8	7.97	58.8	4.03	28.6	2.07, 2.14	$C_{\gamma\gamma'} H$ 2.36, 2.46; $^{13}C_\gamma$ 34.0 $N_{\varepsilon\varepsilon'} H_2$ 6.70, 7.40
His 9	8.02	59.5	4.27	28.6	2.98, 3.26	$C_{\delta 1} H$ 6.98 $C_{\varepsilon 2} H$ 8.02
Leu 10	8.53	57.7	4.18	42.1	1.58, 1.88	$C_\gamma H$ 1.82; $^{13}C_\gamma$ 27.3 $C_\delta H_3$ 0.90; $^{13}C_\delta$ 22.7 $C_{\delta'} H_3$ 0.91; $^{13}C_{\delta'}$ 24.9
Arg 11	8.01	58.3	4.19	30.6	1.92, 1.92	$C_{\gamma\gamma'} H$ 1.69, 1.83; $^{13}C_\gamma$ 27.9 $C_{\delta\delta'} H$ 3.20, 3.20; $^{13}C_\delta$ 43.7 $N_\varepsilon H$ 7.44
Ser 12	7.78	59.7	4.39	64.0	3.93, 3.97	
Ala13	7.83	53.0	4.28	19.3	1.43	
$CONH_2$	6.95, 7.28					

Table ST8. ^{1}H, and ^{13}C chemical shifts (ppm, from DSS) for compound **8** in 30%TFE at 25ºC.

Ac-Ser^{1}-Val^{2}-Arg^{3}-Arg^{4}-Phe^{5}-Leu^{6}-Glu^{7}-Ala^{8}-His^{9}-Leu^{10}-Arg^{11}-Leu^{12}-Ala^{13}-NH$_2$

Residue	HN	$^{13}C_\alpha$	$C_\alpha H$	$^{13}C_\beta$	$C_\beta H$	Others
CH_3CO						CH_3 2.13; ^{13}C 24.7
Ser 1	8.02	59.2	4.47	64.0	3.93, 4.03	
Val 2	8.28	66.0	3.93	32.0	2.15	$C_\gamma H_3$ 1.02; $^{13}C_\gamma$ 20.5
						$C_{\gamma'} H_3$ 1.08; $^{13}C_{\gamma'}$ 22.4
Arg 3	7.98	60.1	4.03	30.2	1.88, 1.92	$C_{\gamma\gamma'}H$ 1.67, 1.74; $^{13}C_\gamma$ nd
						$C_{\delta\delta'}H$ 3.23, 3.23; $^{13}C_\delta$ 43.6
						$N_\varepsilon H$ 7.45
Arg 4	7.86	59.4	4.17	30.3	1.94, 1.94	$C_{\gamma\gamma'}H$ 1.70, 1.77; $^{13}C_\gamma$ 27.4
						$C_{\delta\delta'}H$ 3.24, 3.24; $^{13}C_\delta$ 43.6
						$N_\varepsilon H$ 7.28
Phe 5	7.18	61.6	4.37	39.4	3.28, 3.41	$C_{\delta\delta'}H$ 7.25, 7.25
						$C_{\varepsilon\varepsilon'}H$ 7.18, 7.18
						$C_\zeta H$ ----
Leu 6	8.73	59.0	4.10	42.1	1.68, 1.98	$C_\gamma H$ 1.94; $^{13}C_\gamma$ 27.2
						$C_\delta H_3$ 0.94; $^{13}C_\delta$ 22.8
						$C_{\delta'} H_3$ 0.95; $^{13}C_{\delta'}$ 24.6
Glu 7	8.64	60.3	3.92	29.7	2.10, 2.23	$C_{\gamma\gamma'}H$ 2.28, 2.58; $^{13}C_\gamma$ 37.0
Ala 8	7.98	55.1	4.09	18.0	1.45	
His 9	7.89	59.9	4.19	28.5	3.04, 3.26	$C_{\delta 1}H$ 7.02
						$C_{\varepsilon 2}H$ 7.75
Leu 10	8.42	57.8	4.17	42.1	1.58, 1.91	$C_\gamma H$ 1.83; $^{13}C_\gamma$ 27.2
						$C_\delta H_3$ 0.90; $^{13}C_\delta$ 22.7
						$C_{\delta'} H_3$ 0.92; $^{13}C_{\delta'}$ 24.9
Arg 11	7.97	58.4	4.15	30.3	1.92, 1.92	$C_{\gamma\gamma'}H$ 1.67, 1.81; $^{13}C_\gamma$ 27.9
						$C_{\delta\delta'}H$ 3.21, 3.21; $^{13}C_\delta$ 43.7
						$N_\varepsilon H$ 7.37
Leu 12	7.73	56.4	4.26	42.5	1.59, 1.77	$C_\gamma H$ 1.57; $^{13}C_\gamma$ 27.2
						$C_\delta H_3$ 0.88; $^{13}C_\delta$ 22.9
						$C_{\delta'} H_3$ 0.88; $^{13}C_{\delta'}$ 24.8
Ala13	7.79	53.1	4.24	19.2	1.43	
$CONH_2$	6.90, 7.19					

Table ST9. ^{1}H, and ^{13}C chemical shifts (ppm, from DSS) for compound **15** in 30%TFE at 25ºC.

Ac-Glu^{1}-Val^{2}-Glu^{3}-Lys^{4}-Phe^{5}-Met(O_2)^{6}-Lys^{7}-Val^{8}-Tyr^{9}-Gln^{10}-Arg^{11}-Ser^{12}-Tyr^{13}-NH_2

Residue	HN	$^{13}C_\alpha$	$C_\alpha H$	$^{13}C_\beta$	$C_\beta H$	Others
CH_3CO						CH_3 2.14; ^{13}C 24.5
Glu 1	8.41	58.3	4.23	29.7	2.01, 2.14	$C_{\gamma\gamma'}H$ 2.36, 2.36; $^{13}C_\gamma$ 36.2
Val 2	8.12	65.7	3.85	31.8	2.12	$C_\gamma H_3$ 1.02; $^{13}C_\gamma$ 20.9
						$C_{\gamma'}H_3$ 1.06; $^{13}C_{\gamma'}$ 21.5
Glu 3	8.45	59.6	4.14	29.2	2.04, 2.11	$C_{\gamma\gamma'}H$ 2.33, 2.33; $^{13}C_\gamma$ 36.6
Lys 4	7.81	59.5	4.02	32.4	1.89, 1.89	$C_{\gamma\gamma'}H$ 1.34, 1.49; $^{13}C_\gamma$ 25.0
						$C_{\delta\delta'}H$ 1.69, 1.69; $^{13}C_\delta$ 29.4
						$C_{\varepsilon\varepsilon'}H$ 2.92, 2.92; $^{13}C_\varepsilon$ 42.1
Phe 5	8.15	nd	4.32	38.8	3.25, 3.25	$C_{\delta\delta'}H$ 7.22, 7.22
						$C_{\varepsilon\varepsilon'}H$ 7.25, 7.25
						$C_\zeta H$ 7.35
Met(O_2) 6	8.48	58.0	4.15	25.6	2.40, 2.50	$C_{\gamma\gamma'}H$ 3.27, 3.57; $^{13}C_\gamma$ 53.3
						$C_\varepsilon H_3$ 3.01; $^{13}C_\varepsilon$ 42.6
Lys 7	7.99	58.9	4.16	32.5	1.90, 2.01	$C_{\gamma\gamma'}H$ 1.49, 1.66; $^{13}C_\gamma$ 25.4
						$C_{\delta\delta'}H$ 1.70, 1.70; $^{13}C_\delta$ 29.1
						$C_{\varepsilon\varepsilon'}H$ 2.98, 2.98; $^{13}C_\varepsilon$ 42.2
Val 8	7.98	65.5	3.75	32.1	2.07	$C_\gamma H_3$ 0.81; $^{13}C_\gamma$ 20.6
						$C_{\gamma'}H_3$ 1.00; $^{13}C_{\gamma'}$ 21.5
Tyr 9	8.38	60.6	4.20	38.4	2.72, 2.97	$C_{\delta\delta'}H$ 7.00, 7.00
						$C_{\varepsilon\varepsilon'}H$ 6.74, 6.74
Gln 10	8.12	57.7	4.11	28.8	2.17, 2.17	$C_{\gamma\gamma'}H$ 2.41, 2.52; $^{13}C_\gamma$ 34.0
						$N_{\varepsilon\varepsilon'}H_2$ 6.72, 7.32
Arg 11	7.91	57.2	4.23	30.4	1.87, 1.90	$C_{\gamma\gamma'}H$ 1.70, 1.70; $^{13}C_\gamma$ 27.1
						$C_{\delta\delta'}H$ 3.19, 3.19; $^{13}C_\delta$ 43.3
						$N_\varepsilon H$ 7.20
Ser 12	7.95	59.6	4.33	63.8	3.61, 3.72	
Tyr 13	7.93	nd	4.48	39.0	2.65, 3.03	$C_{\delta\delta'}H$ 7.01, 7.01
						$C_{\varepsilon\varepsilon'}H$ 6.78, 6.78
$CONH_2$	6.97, 7.28					

Table ST10. ^{1}H, and ^{13}C chemical shifts (ppm, from DSS) for compound **16** in 30%TFE at 25ºC

Ac-Glu^{1}-Val^{2}-c$^{3-7}$[Glu^{3}-Lys^{4}-Phe^{5}-Met(O$_2$)^{6}-Lys^{7}]-Val^{8}-Tyr^{9}-Gln^{10}-Arg^{11}-Ser^{12}-Tyr^{13}-NH$_2$

Residue	HN	$^{13}C_\alpha$	$C_\alpha H$	$^{13}C_\beta$	$C_\beta H$	Others
CH_3CO						CH_3 2.17; ^{13}C 24.7
Glu 1	8.46	57.9	4.19	29.4	2.03, 2.13	$C_{\gamma\gamma'}H$ 2.42, 2.42; $^{13}C_\gamma$ 36.2
Val 2	8.03	66.3	3.82	32.2	2.10	$C_\gamma H_3$ 1.02; $^{13}C_\gamma$ 21.0
						$C_{\gamma'}H_3$ 1.07; $^{13}C_{\gamma'}$ 22.0
Glu 3	7.88	60.6	4.10	27.5	1.94, 2.44	$C_{\gamma\gamma'}H$ 2.41, 2.60; $^{13}C_\gamma$ 34.9
Lys 4	7.56	60.1	3.86	32.3	1.90, 1.96	$C_{\gamma\gamma'}H$ 1.46, 1.61; $^{13}C_\gamma$ 25.5
						$C_{\delta\delta'}H$ 1.73, 1.73; $^{13}C_\delta$ 29.4
						$C_{\varepsilon\varepsilon'}H$ 2.99, 2.99; $^{13}C_\varepsilon$ 42.5
Phe 5	8.14	61.5	4.25	38.8	3.26, 3.26	$C_{\delta\delta'}H$ 7.18, 7.18
						$C_{\varepsilon\varepsilon'}H$ 7.23, 7.23
						$C_\zeta H$ 7.24
Met(O$_2$) 6	8.46	60.6	4.04	25.3	2.45, 2.70	$C_{\gamma\gamma'}H$ 3.28, 3.71; $^{13}C_\gamma$ 53.6
						$C_\varepsilon H_3$ 3.01; $^{13}C_\varepsilon$ 42.9
Lys 7	7.97	59.0	4.04	33.7	1.87, 1.92	$C_{\gamma\gamma'}H$ 1.24, 1.94; $^{13}C_\gamma$ 26.6
						$C_{\delta\delta'}H$ 1.43, 1.57; $^{13}C_\delta$ 31.0
						$C_{\varepsilon\varepsilon'}H$ 2.69, 3.57; $^{13}C_\varepsilon$ 42.6
						$N_\zeta H$ 7.57
Val 8	8.10	66.6	3.63	32.0	2.10	$C_\gamma H_3$ 0.83; $^{13}C_\gamma$ 20.9
						$C_{\gamma'}H_3$ 1.05; $^{13}C_{\gamma'}$ 22.2
Tyr 9	8.63	61.9	4.07	38.6	2.69, 2.98	$C_{\delta\delta'}H$ 6.99, 6.99
						$C_{\varepsilon\varepsilon'}H$ 6.72, 6.72
Gln 10	8.30	58.6	4.06	28.8	2.21, 2.25	$C_{\gamma\gamma'}H$ 2.47, 2.59; $^{13}C_\gamma$ 34.4
						$N_{\varepsilon\varepsilon'}H_2$ 6.68, 7.29
Arg 11	7.88	58.8	4.19	30.4	1.91, 1.95	$C_{\gamma\gamma'}H$ 1.72, 1.76; $^{13}C_\gamma$ 27.4
						$C_{\delta\delta'}H$ 3.19, 3.19; $^{13}C_\delta$ 43.5
						$N_\varepsilon H$ 7.21
Ser 12	7.89	60.4	4.29	64.0	3.53, 3.67	
Tyr 13	7.90	58.6	4.45	39.2	2.54, 3.01	$C_{\delta\delta'}H$ 6.95, 6.95
						$C_{\varepsilon\varepsilon'}H$ 6.75, 6.75
$CONH_2$	6.96, 7.26					

Table ST11. ^{1}H, and ^{13}C chemical shifts (ppm, from DSS) for compound **17** in 30%TFE at 25ºC

Ac-Glu^{1}-Val^{2}-Val^{3}-Lys^{4}-Phe^{5}-Met(O_2)^{6}-Glu^{7}-Val^{8}-Tyr^{9}-Gln^{10}-Lys^{11}-Ser^{12}-Tyr^{13}-NH_2

Residue	HN	$^{13}C_\alpha$	$C_\alpha H$	$^{13}C_\beta$	$C_\beta H$	Others
CH_3CO						CH_3 2.10, ^{13}C 24.3
Glu 1	8.44		4.18		1.99, 2.08	$C_{\gamma\gamma'}H$ 2.34, 2.34
Val 2	8.07		3.97		2.13	$C_\gamma H_3$ 1.00; $^{13}C_\gamma$ 20.7
						$C_{\gamma'}H_3$ 1.05; $^{13}C_{\gamma'}$ 21.1
Val 3	7.62		3.96		2.12	$C_\gamma H_3$ 0.98; $^{13}C_\gamma$ 20.9
						$C_{\gamma'}H_3$ 1.03; $^{13}C_{\gamma'}$ 21.5
Lys 4	7.78		4.21		1.88, 1.88	$C_{\gamma\gamma'}H$ 1.42, 1.47
						$C_{\delta\delta'}H$ 1.70, 1.70
						$C_{\varepsilon\varepsilon'}H$ 2.94, 2.94; $^{13}C_\varepsilon$ 42.0
Phe 5	8.16		4.36		3.21, 3.21	$C_{\delta\delta'}H$ 7.21, 7.21
						$C_{\varepsilon\varepsilon'}H$ 7.28, 7.28
						$C_\zeta H$ 7.30
Met(O_2) 6	8.36		4.16		2.39, 2.52	$C_{\gamma\gamma'}H$ 3.26, 3.55
						$C_\varepsilon H_3$ 3.01; $^{13}C_\varepsilon$ 42.5
Glu 7	8.20		4.13		2.14, 2.23	$C_{\gamma\gamma'}H$ 2.44, 2.44
Val 8	7.97		3.73		2.10	$C_\gamma H_3$ 0.86; $^{13}C_\gamma$ 20.7
						$C_{\gamma'}H_3$ 1.03; $^{13}C_{\gamma'}$ 21.6
Tyr 9	8.41		4.17		2.79, 3.00	$C_{\delta\delta'}H$ 7.03, 7.03
						$C_{\varepsilon\varepsilon'}H$ 6.75, 6.75
Gln 10	8.24		4.09		2.19, 2.19	$C_{\gamma\gamma'}H$ 2.45, 2.54
						$N_{\varepsilon\varepsilon'}H_2$ 6.73, 7.29
Lys 11	7.98		4.19		1.88, 1.88	$C_{\gamma\gamma'}H$ 1.47, 1.57;
						$C_{\delta\delta'}H$ 1.69, 1.69
						$C_{\varepsilon\varepsilon'}H$ 2.99, 2.99; $^{13}C_\varepsilon$ 42.2
Ser 12	7.90		4.30		3.57, 3.71	
Tyr 13	7.90		4.46		2.60, 3.02	$C_{\delta\delta'}H$ 6.99, 6.99
						$C_{\varepsilon\varepsilon'}H$ 6.77, 6.77
$CONH_2$	6.97, 7.30					

Table ST12. ^{1}H, and ^{13}C chemical shifts (ppm, from DSS) for compound **18** in 30%TFE at 25ºC

Ac-Glu^{1}-Val^{2}-Val^{3}-Lys^{4}-Phe^{5}-Met(O_2)^{6}-c$^{7\text{-}11}$[Glu^{7}-Val^{8}-Tyr^{9}-Gln^{10}-Lys^{11}]-Ser^{12}-Tyr^{13}-NH_2

Residue	HN	$^{13}C_\alpha$	$C_\alpha H$	$^{13}C_\beta$	$C_\beta H$	Others
CH_3CO						CH_3 1.96, ^{13}C 24.5
Glu 1	8.24	58.8	3.98	29.3	1.86, 1.92	$C_{\gamma\gamma'}H$ 2.24, 2.24; $^{13}C_\gamma$ 35.2
Val 2	7.80	65.7	3.76	32.1	1.97	$C_\gamma H_3$ 0.86; $^{13}C_\gamma$ 20.8
						$C_{\gamma'}H_3$ 0.91; $^{13}C_{\gamma'}$ 21.5
Val 3	7.28	65.8	3.75	32.0	1.98	$C_\gamma H_3$ 0.83; $^{13}C_\gamma$ 20.9
						$C_{\gamma'}H_3$ 0.88; $^{13}C_{\gamma'}$ 21.8
Lys 4	7.48	59.3	4.03	32.5	1.77, 1.77	$C_{\gamma\gamma'}H$ 1.28, 1.36; $^{13}C_\gamma$ 25.1
						$C_{\delta\delta'}H$ 1.53, 1.65; $^{13}C_\delta$ 29.5
						$C_{\varepsilon\varepsilon'}H$ 2.77, 2.77; $^{13}C_\varepsilon$ 42.4
Phe 5	8.02	61.2	4.16	38.9	3.07, 3.07	$C_{\delta\delta'}H$ 7.02, 7.02
						$C_{\varepsilon\varepsilon'}H$ 7.10, 7.10
						$C_\zeta H$ 7.07
Met(O_2) 6	8.22	58.8	3.89	25.7	2.23, 2.41	$C_{\gamma\gamma'}H$ 3.06, 3.48; $^{13}C_\gamma$ 53.7
						$C_\varepsilon H_3$ 2.79; $^{13}C_\varepsilon$ 42.7
Glu 7	8.00	61.3	3.86	28.0	1.86, 2.56	$C_{\gamma\gamma'}H$ 2.23, 2.37; $^{13}C_\gamma$ 35.4
Val 8	7.83	66.9	3.35	32.0	1.99	$C_\gamma H_3$ 0.78; $^{13}C_\gamma$ 21.0
						$C_{\gamma'}H_3$ 0.98; $^{13}C_{\gamma'}$ 22.7
Tyr 9	8.40	nd	3.82	38.5	2.65, 2.93	$C_{\delta\delta'}H$ 6.85, 6.85
						$C_{\varepsilon\varepsilon'}H$ 6.54, 6.54
Gln 10	8.16	59.5	3.83	28.6	2.15, 2.21	$C_{\gamma\gamma'}H$ 2.34, 2.51; $^{13}C_\gamma$ 34.5
						$N_{\varepsilon\varepsilon'}H_2$ 6.50, 7.06
Lys 11	7.87	60.0	3.84	34.2	1.61, 1.70	$C_{\gamma\gamma'}H$ 1.07, 1.74; $^{13}C_\gamma$ 26.6
						$C_{\delta\delta'}H$ 1.28, 1.34; $^{13}C_\delta$ 30.9
						$C_{\varepsilon\varepsilon'}H$ 2.53, 3.34; $^{13}C_\varepsilon$ 42.4
						$N_\zeta H$ 7.34
Ser 12	7.66	61.0	4.02	64.0	3.24, 3.47	
Tyr 13	7.76	58.9	4.24	39.3	2.22, 2.82	$C_{\delta\delta'}H$ 6.70, 6.70
						$C_{\varepsilon\varepsilon'}H$ 6.54, 6.54
$CONH_2$	6.78, 7.09					

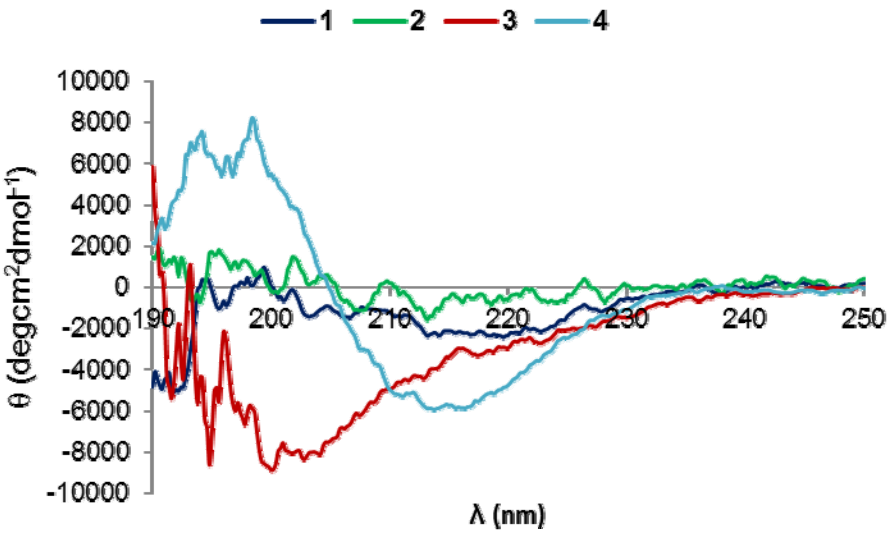
Table ST13. Structural statistics for the 20 lowest target function structures calculated for analogues **1-8**, **15-18**.

Peptide	Restraints		RMSD[b]	
	Distance[a]	Dihedral	Backbone atoms	All heavy atoms
1	50	24	0.4 ± 0.2	1.9 ± 0.2
2	57	24	0.2 ± 0.1	1.4 ± 0.2
3	25	23	0.4 ± 0.1	1.6 ± 0.2
4	38	23	0.4 ± 0.1	1.6 ± 0.2
5	31	20	0.3 ± 0.2	1.6 ± 0.2
6	62	22	0.1 ± 0.1	1.8 ± 0.3
7	64	22	0.1 ± 0.1	1.5 ± 0.2
8	59	22	0.1 ± 0.1	1.6 ± 0.2
15	42	24	0.5 ± 0.3	1.8 ± 0.3
16	54	22	0.2 ± 0.1	1.5 ± 0.2
17	16	24	0.5 ± 0.2	1.7 ± 0.2
18	55	22	0.2 ± 0.2	1.2 ± 0.2

[a]Non-sequential and the sequential amide – amide ($d_{NN(i,i+1)}$). [b]Excluding N- and C-terminal residues

Figure S1: CD graphics in A) H_2O and B) 30% TFE/H_2O, for $VEGF_{13-25}$ analogues **1-4**.

A)



B)

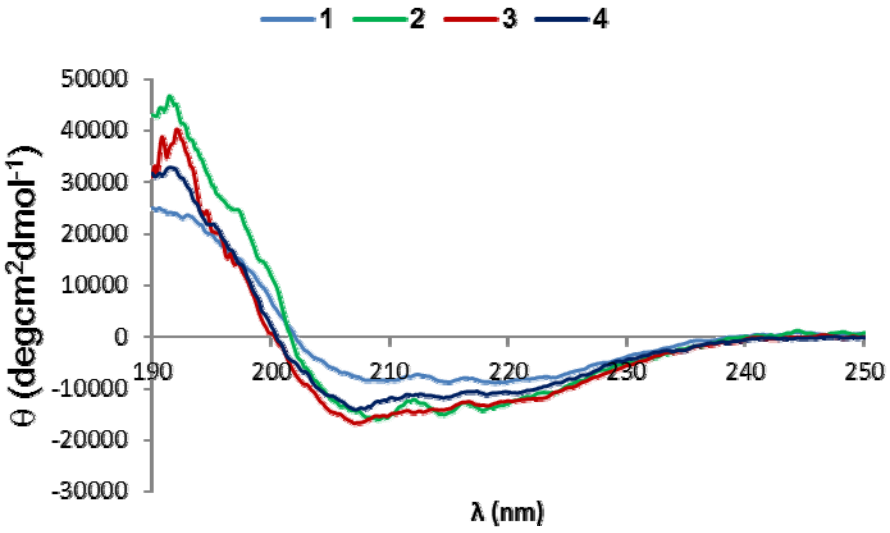
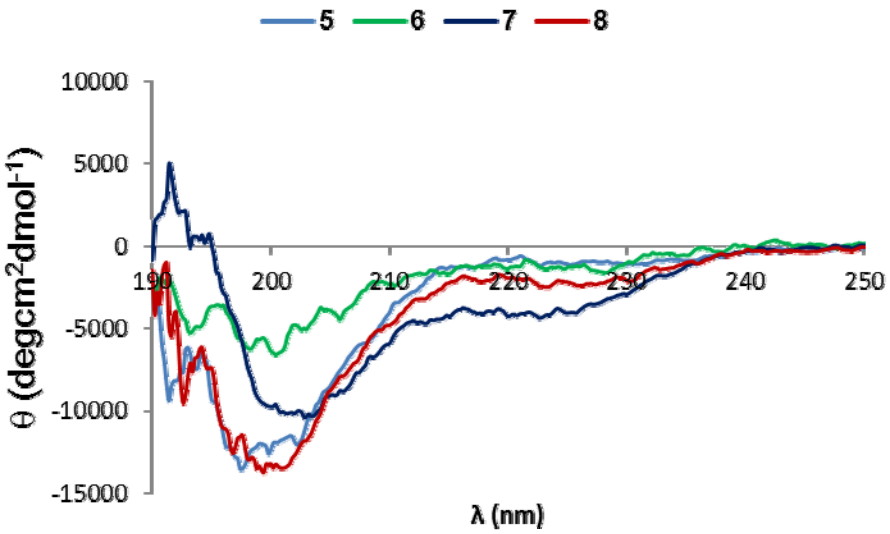


Figure S2: CD graphics in A) H_2O and B) 30% TFE/H_2O, for Vammin$_{1\text{-}13}$ analogues **5-8**.

A)



B)

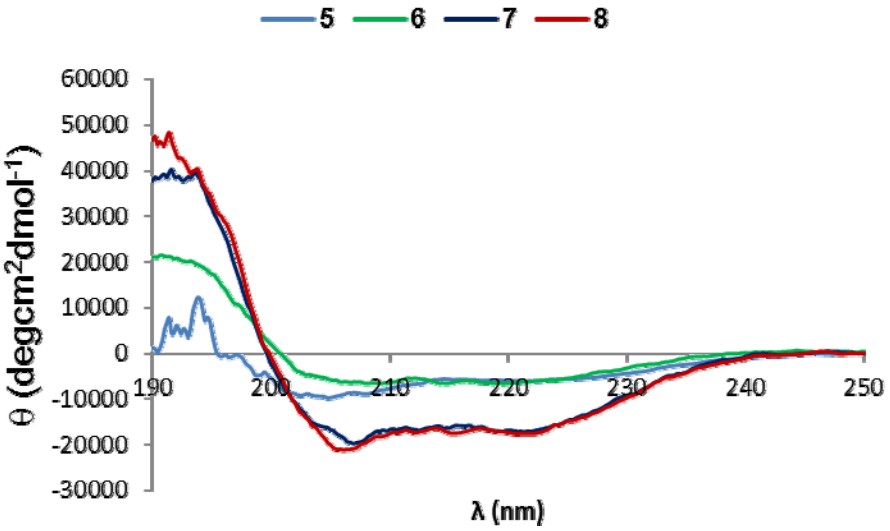
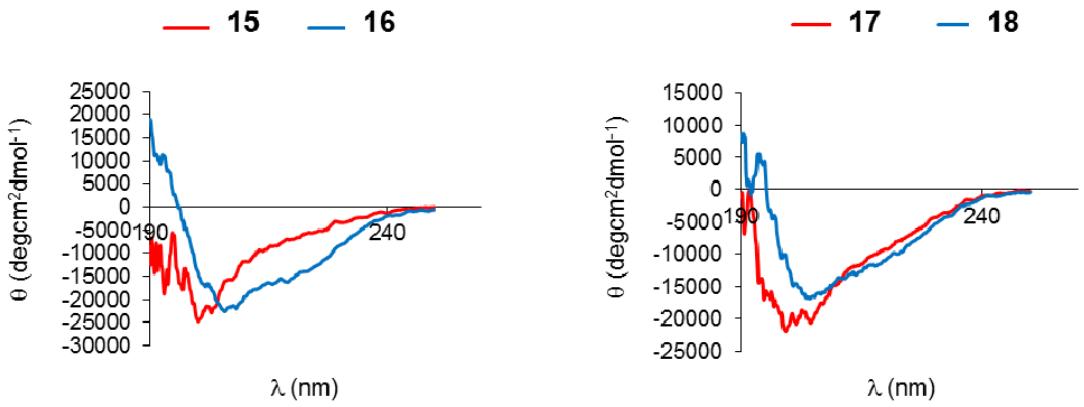


Figure S3: CD graphics in A) H_2O and B) 30% TFE/H_2O, for $VEGF_{13-25}$ analogues **15-18**.

A)



B)

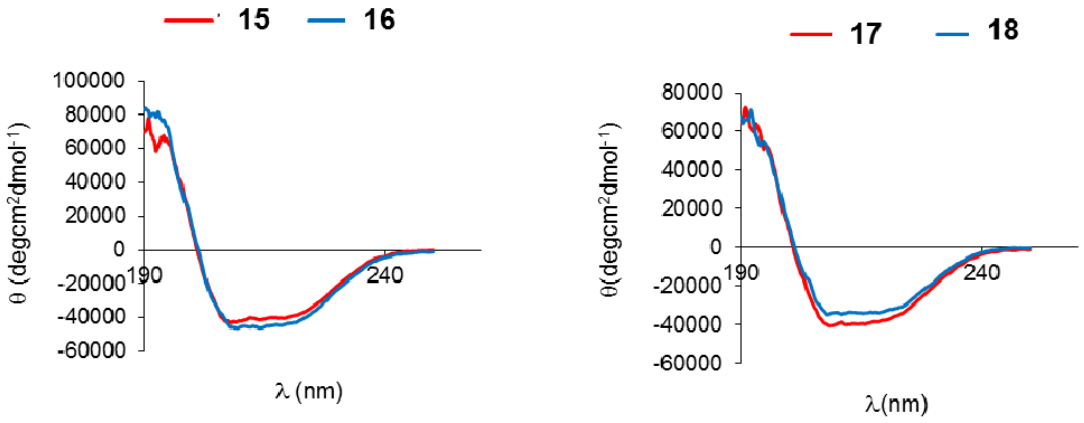


Figure S4. $\Delta\delta_{C\alpha}$ observed for $VEGF_{13\text{-}25}$ analogues **1**-**4**. Missing bars correspond to residues whose Cα chemical shift was not assigned.

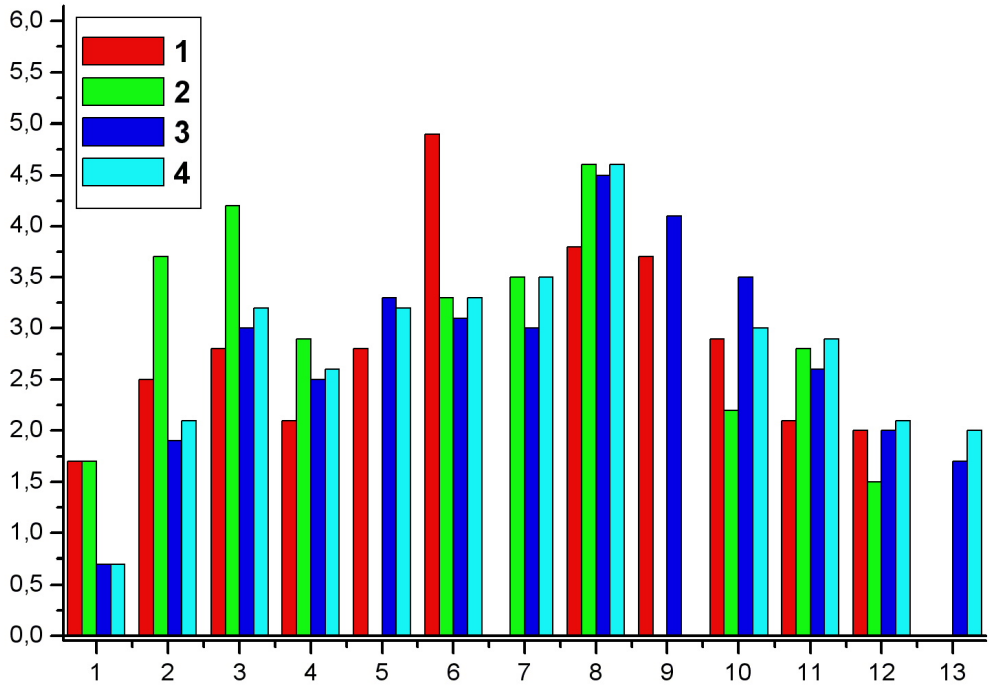


Figure S5. $\Delta\delta_{C\alpha}$ observed for Vammin$_{1\text{-}13}$ analogues **5-8**. Missing bars correspond to residues whose Cα chemical shift was not assigned.

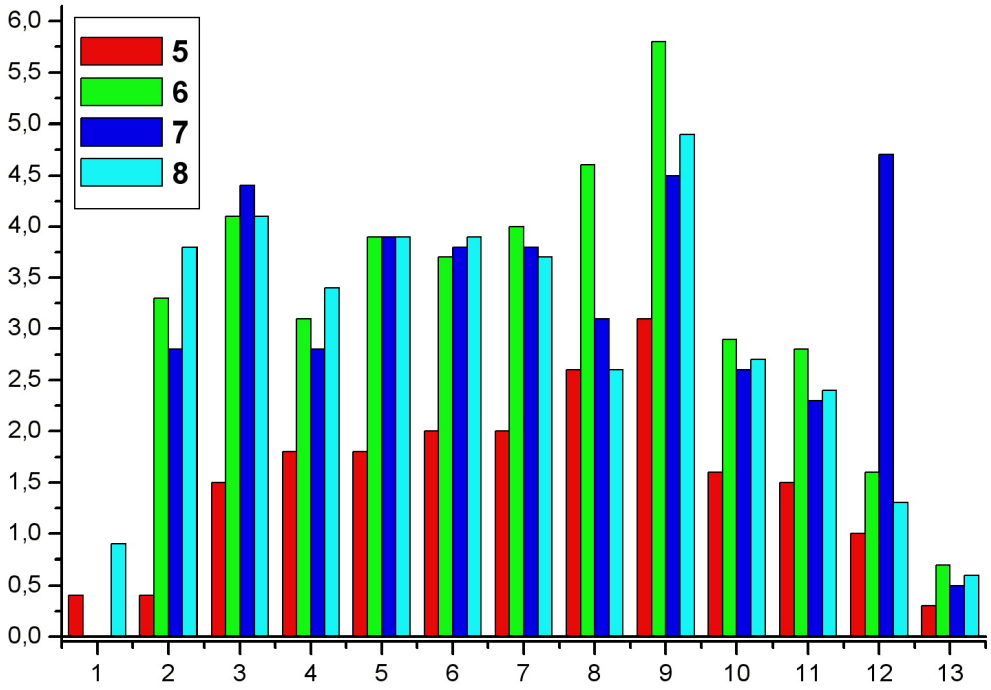


Figure S6. $\Delta\delta_{C\alpha}$ observed for linear and cyclic $VEGF_{13\text{-}25}$ analogues **15-18**. Missing bars correspond to residues whose Cα chemical shift was not assigned.

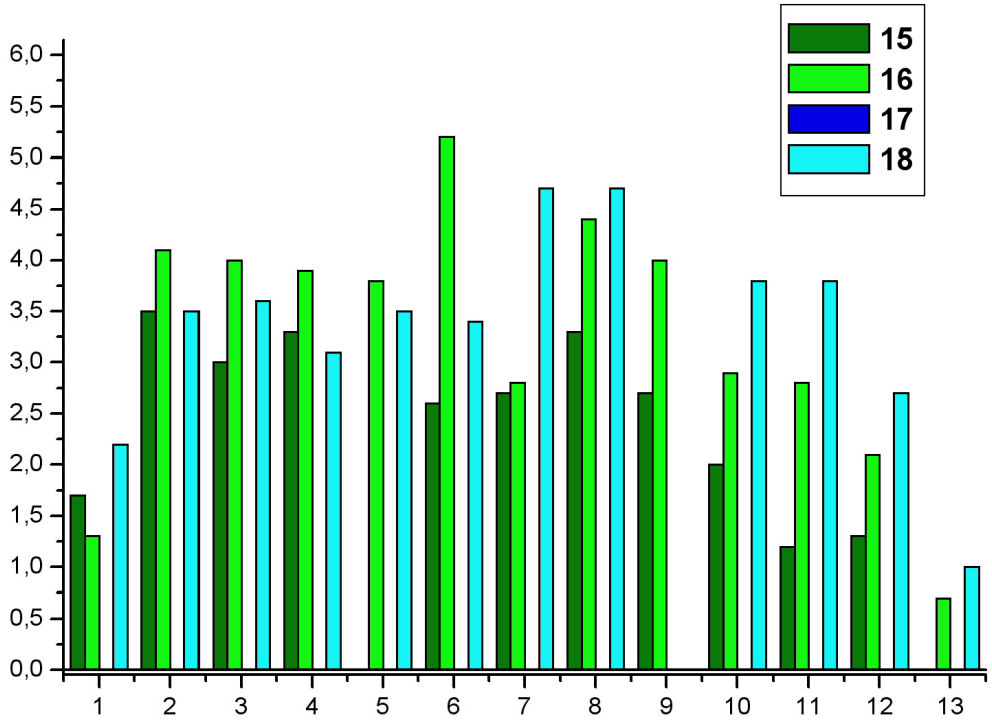


Figure S7. NOE summaries of $VEGF_{13-25}$ analogues **1**-**4** in 30% TFE at 25ºC. N- and C-termini are, respectively, in acetylated and amidated. The thickness of the lines indicates the intensities of the sequential NOEs, i.e., strong, medium, weak.

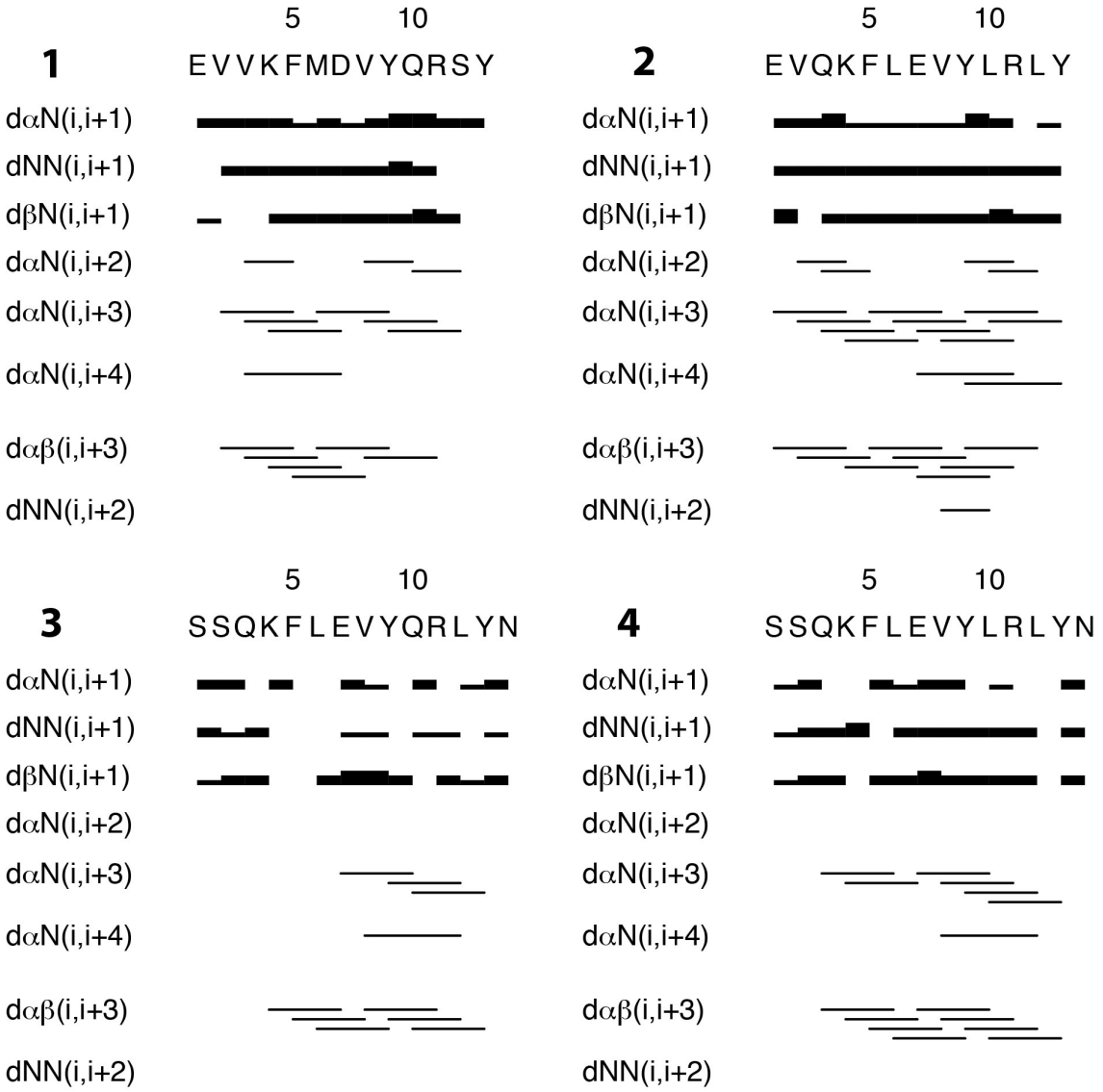


Figure S8. NOE summaries of Vammin$_{1\text{-}13}$ analogues **5-8** in 30% TFE at 25ºC. N- and C-termini are, respectively, in acetylated and amidated. The thickness of the lines indicates the intensities of the sequential NOEs, i.e., strong, medium, weak.

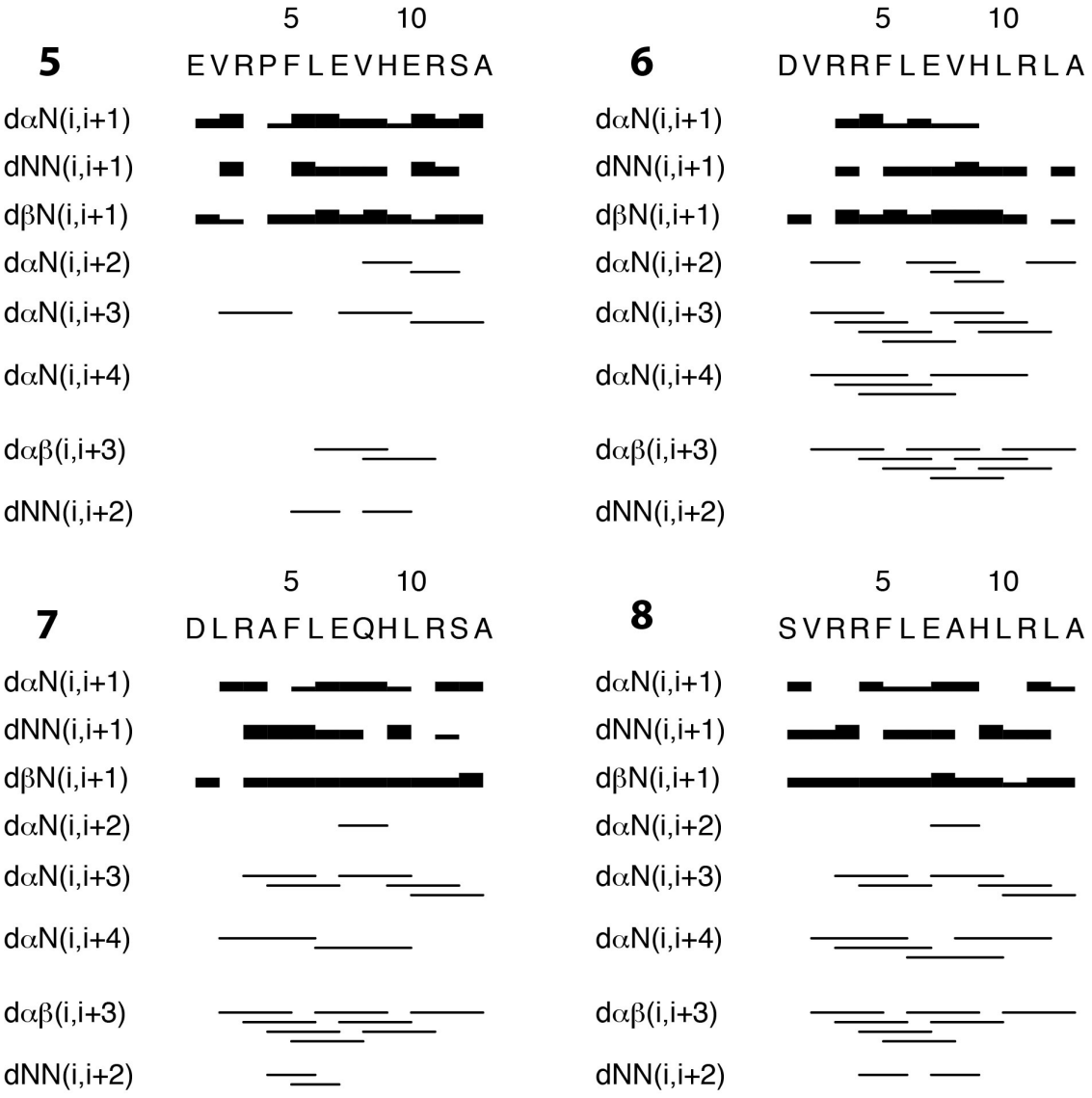


Figure S9. NOE summaries of $VEGF_{13-25}$ analogues **15-18** in 30% TFE at 25ºC. N- and C-termini are, respectively, in acetylated and amidated. The thickness of the lines indicates the intensities of the sequential NOEs, i.e., strong, medium, weak.

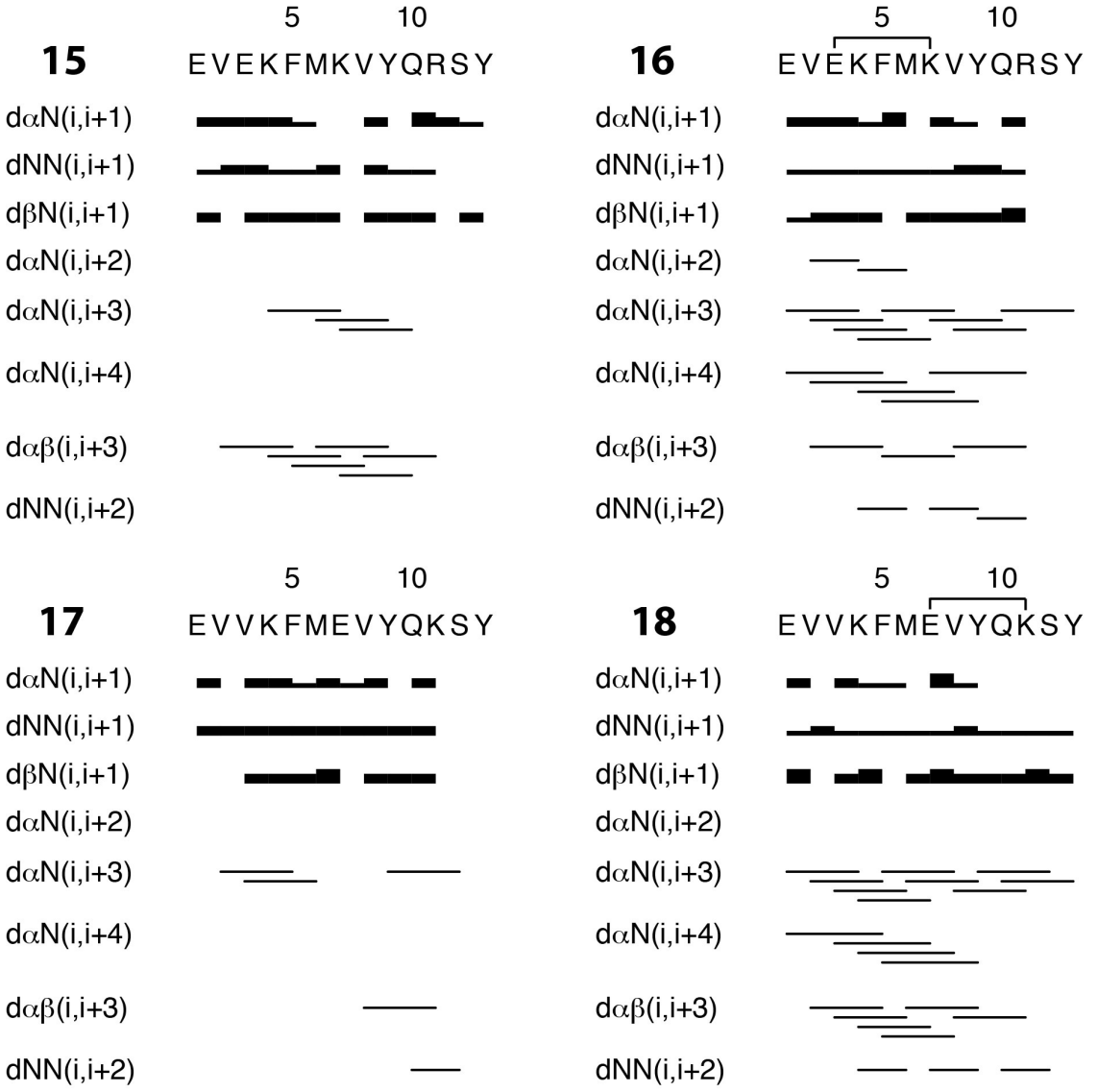
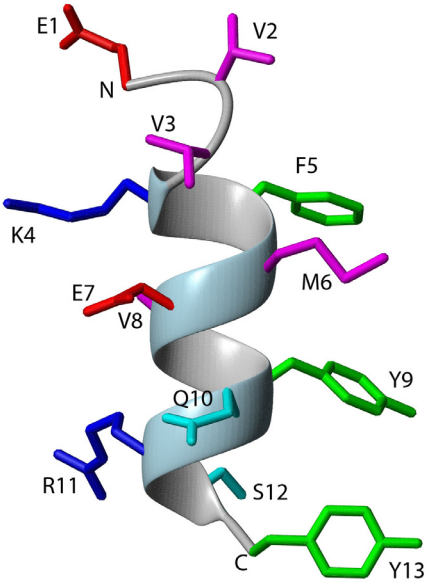
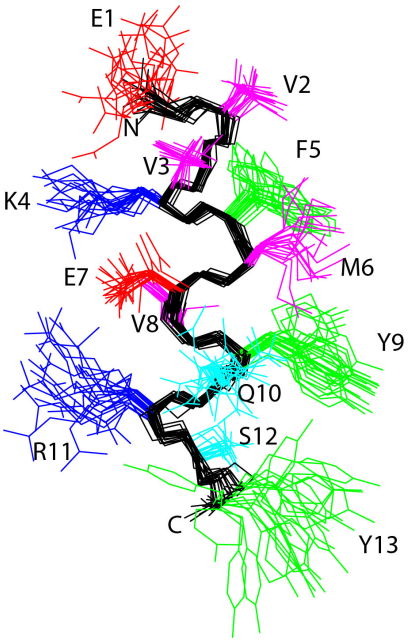


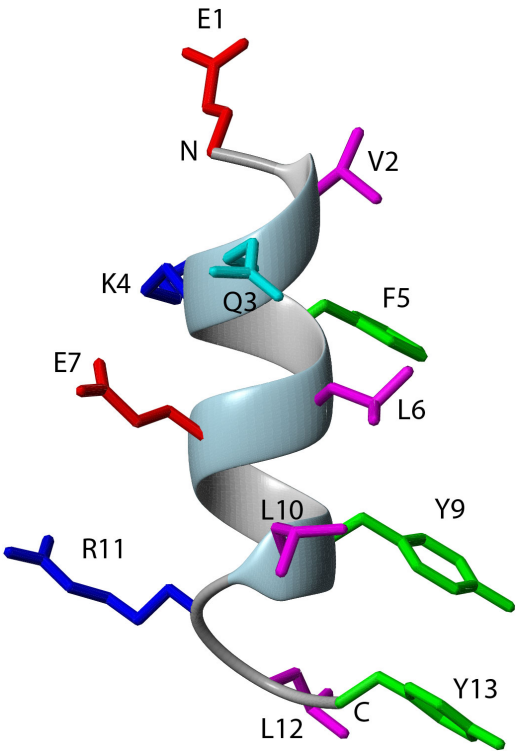
Figure S10. NMR structures of VEGF and Vammin analogues: (Left) Ribbon representation of the calculated structure with the lowest target function. For some peptides the side chains of one or two are not seen because they lie behind the ribbon. (Right) Superposition of the 20 NMR calculated structures. Backbone atoms are shown in black. Side chains are colored in red for the negatively charged residues (Glu/Asp), in blue for the positively charged residues (Lys/Arg), in cyan for the polar residues (Ser/Gln/Asn), in magenta for the hydrophobic residues (Val/Leu/Met), and in green for the residues reported as key for the interaction with VEGF receptors (F5, Y9 & Y13 in VEGF analogues and the equivalent residues F5, H9 & A13 in Vammin analogues). Hydrogen atoms are not shown. All the residues are labeled and the N- and C-ends are indicated.

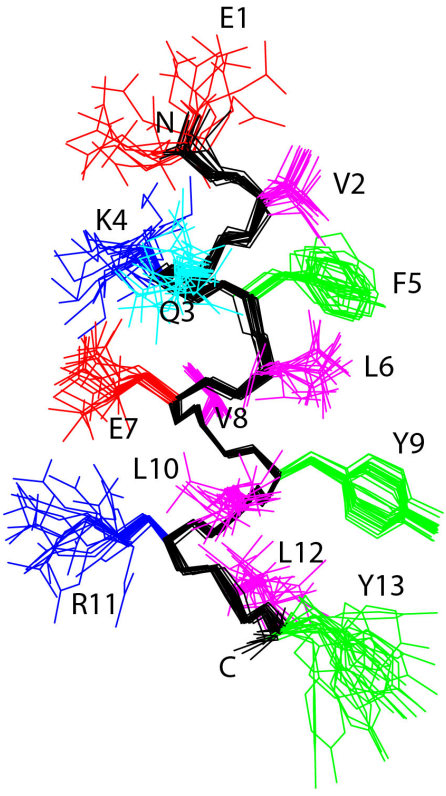
Peptide 1



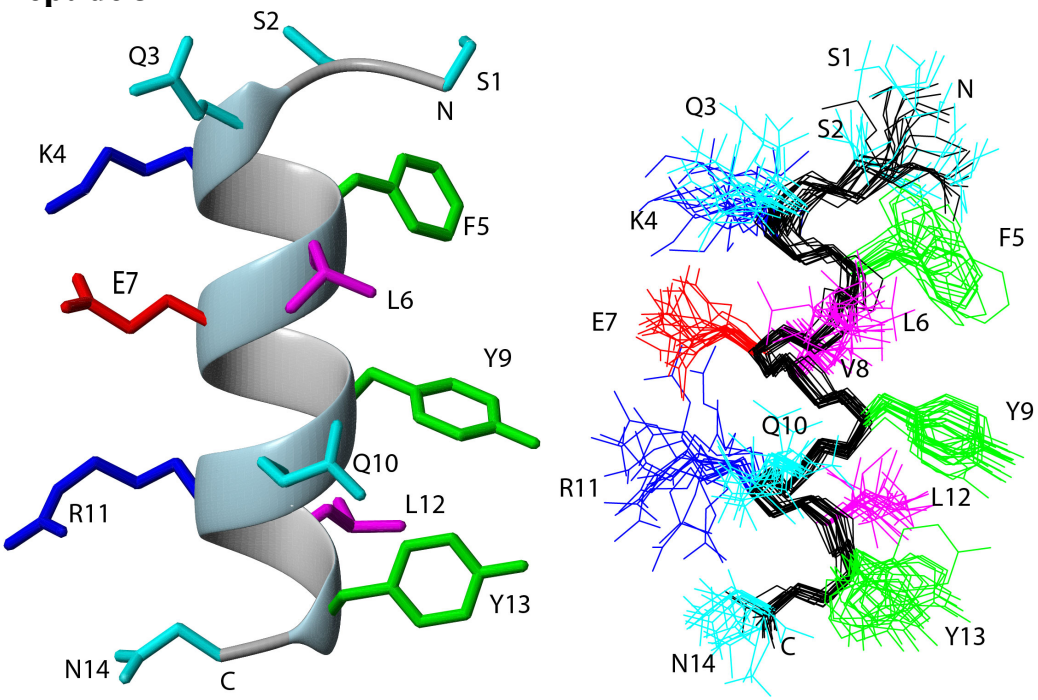


Peptide 2





Peptide 3



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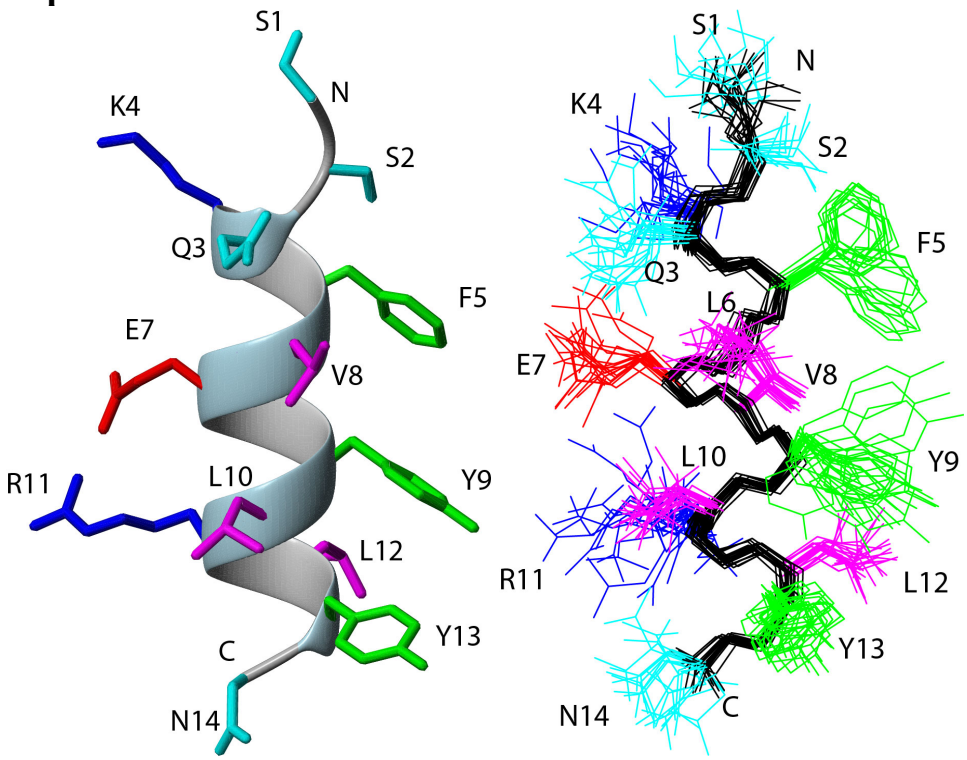
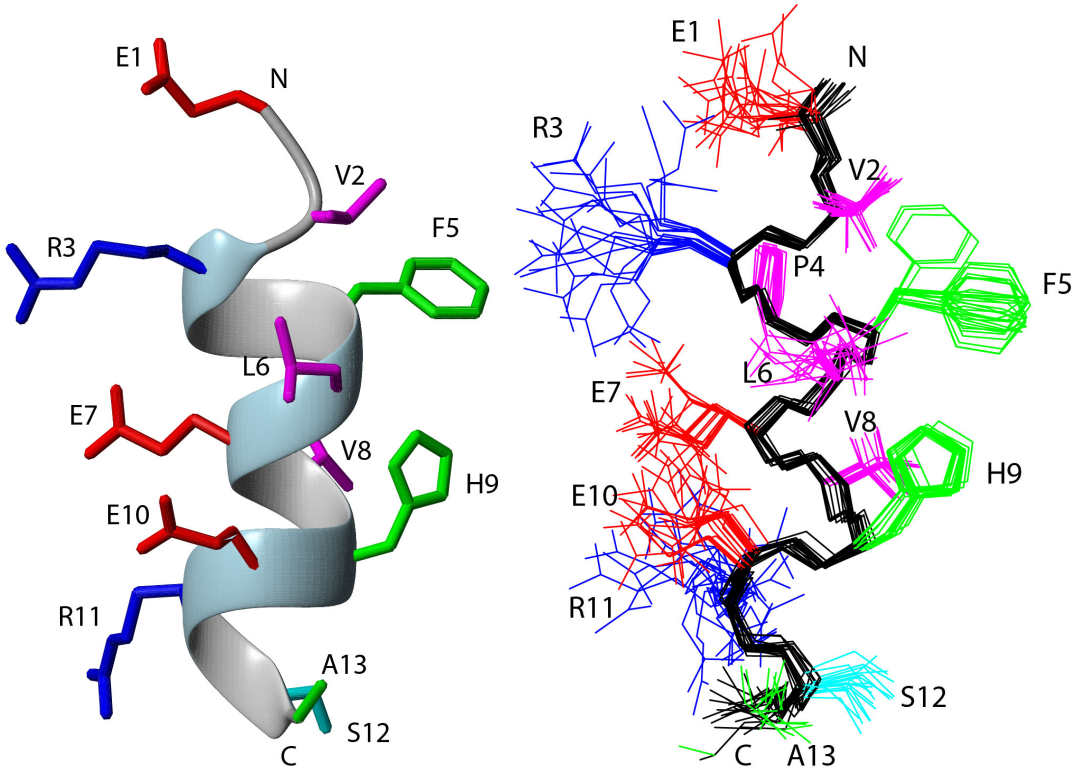
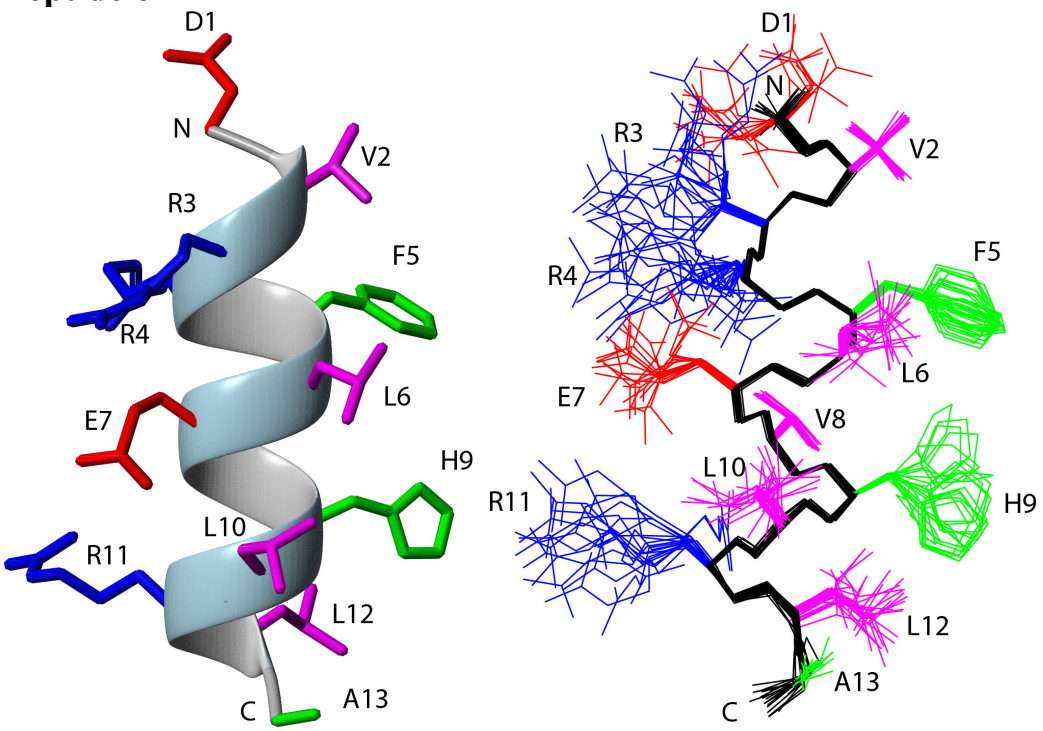


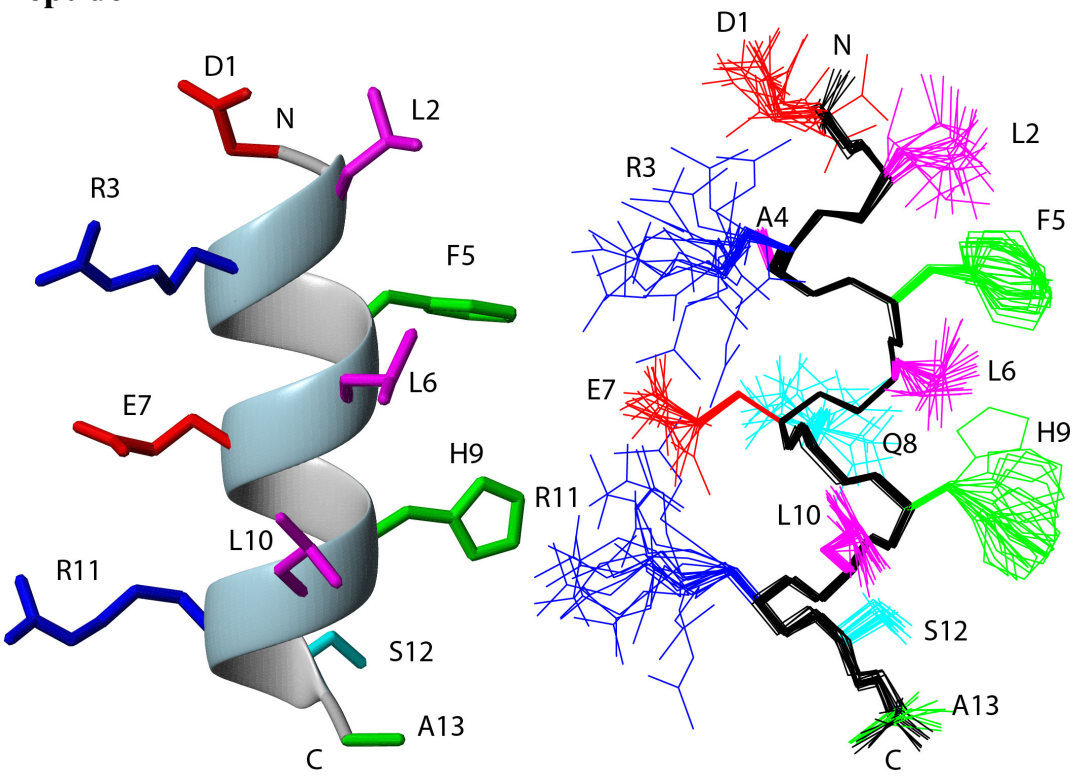
Peptide 5



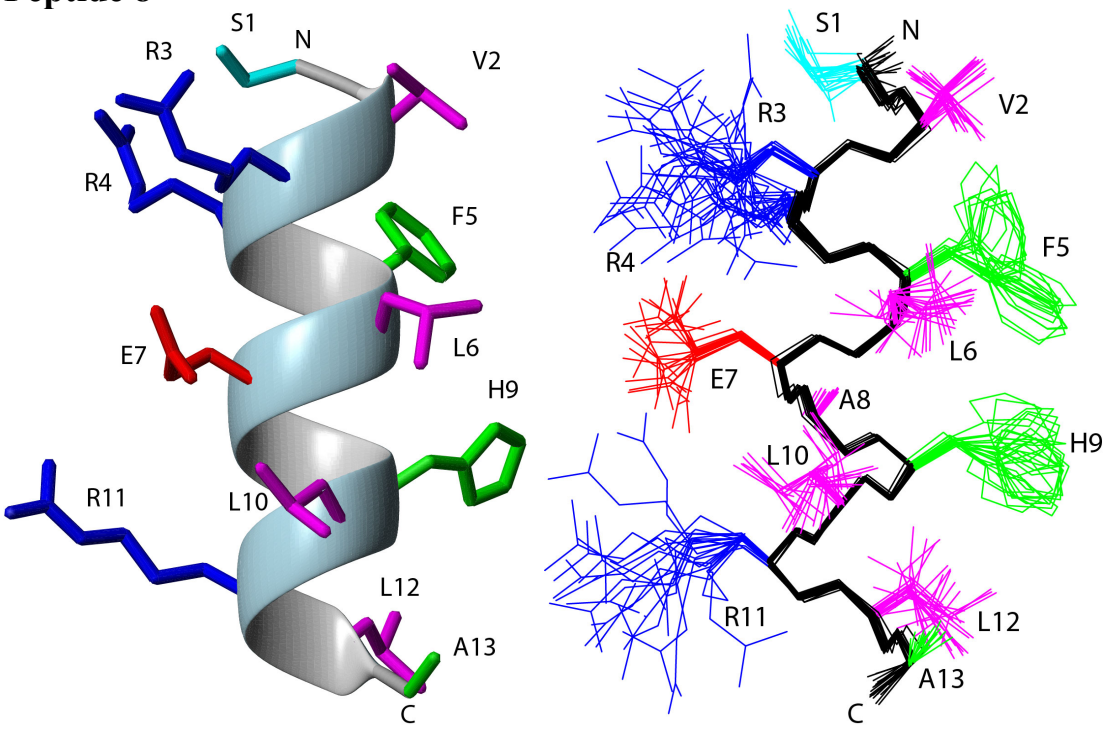
Peptide 6



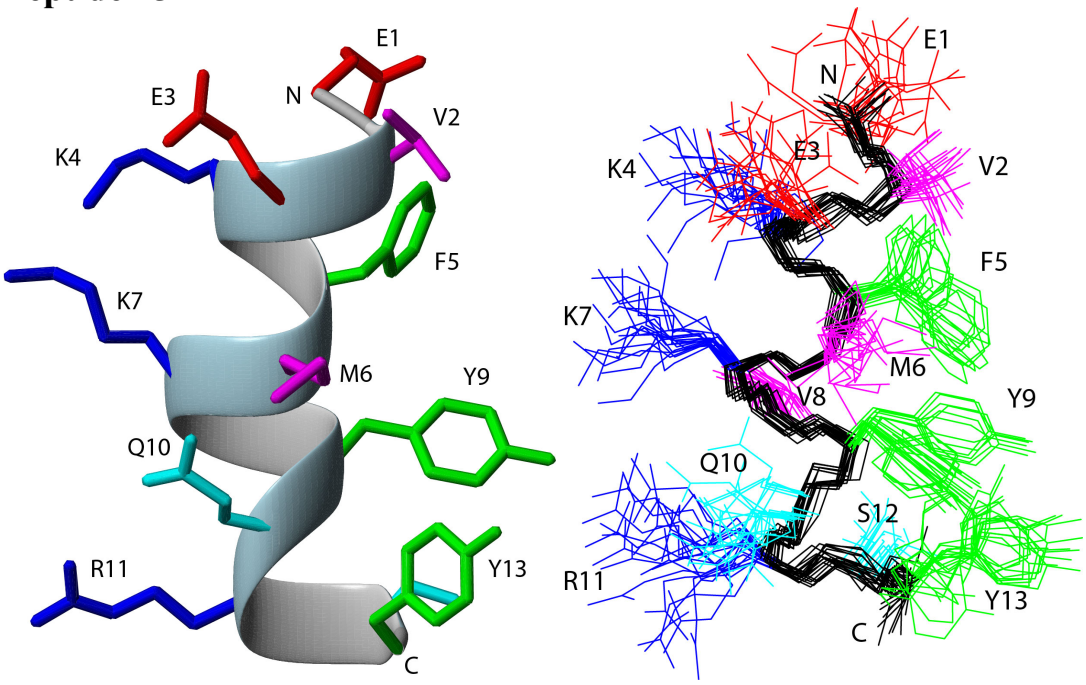
Peptide 7



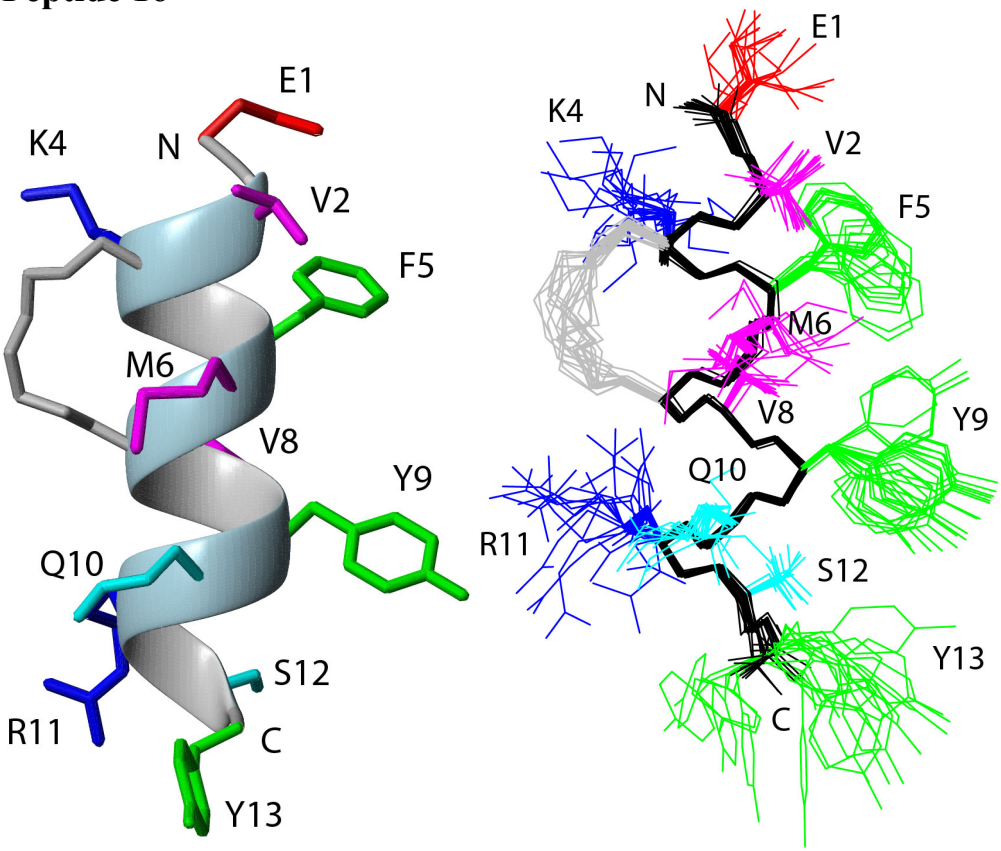
Peptide 8



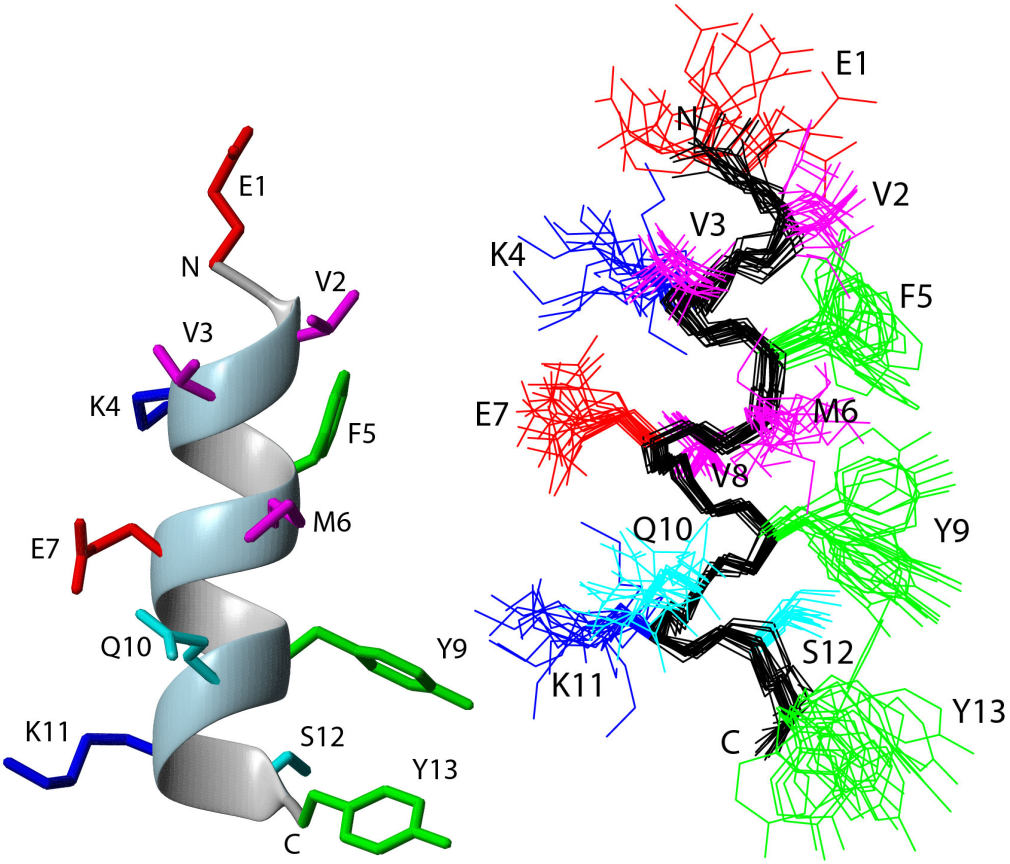
Peptide 15



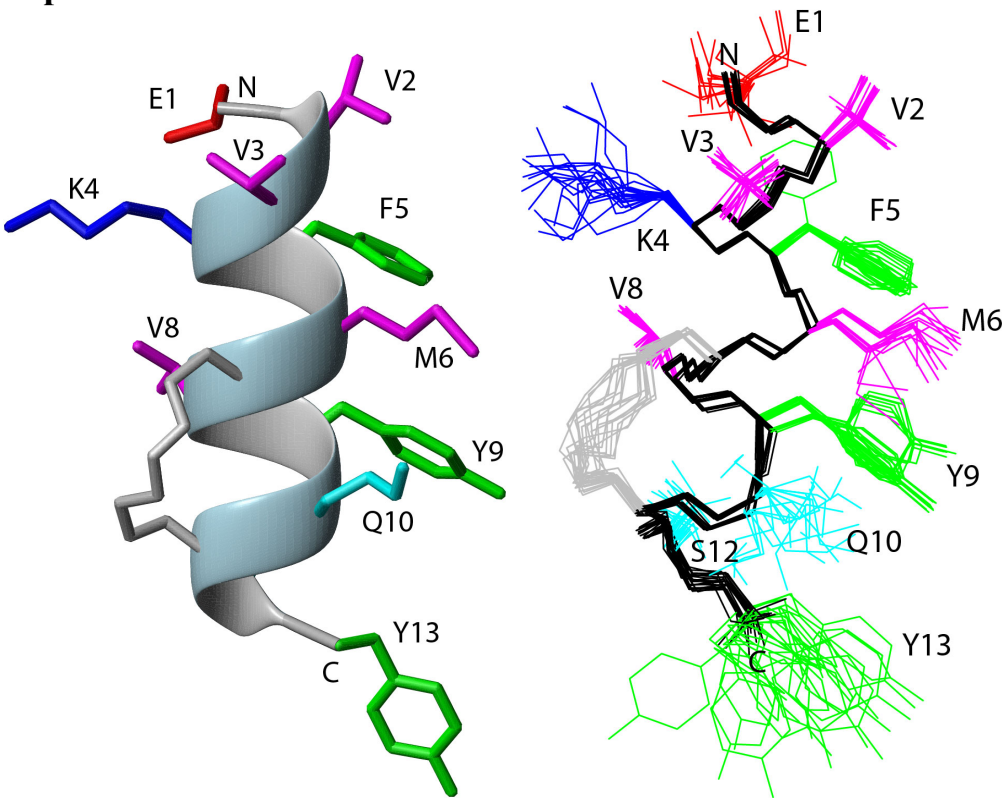
Peptide 16



Peptide 17



Peptide 18



Chemiluminescent competition assays. **Reagents and materials**. High-binding 96-well microplates were from Corning Life Sciences, Netherlands. Recombinant human VEGFR-1 ECD/Fc Chimera, VEGFR-1 D1-D3/Fc chimera and bt$VEGF_{165}$ obtained as part of a Fluorokine biotinylated VEGF kit, were from R&D Systems, UK. Bovine serum albumin fraction V, BSA was from Sigma-Aldrich, France. AMDEX streptavidin-horseradish peroxidase was from Amersham Biosciences, UK, SuperSignal West Pico Chemiluminescent Substrate from Pierce, USA. Luminescence was quantified with an EnVision 2101 Multilabel Reader from PerkinElmer, USA. Data were analyzed using GraphPad Prism software version 4.03, USA.