Supplemental Information

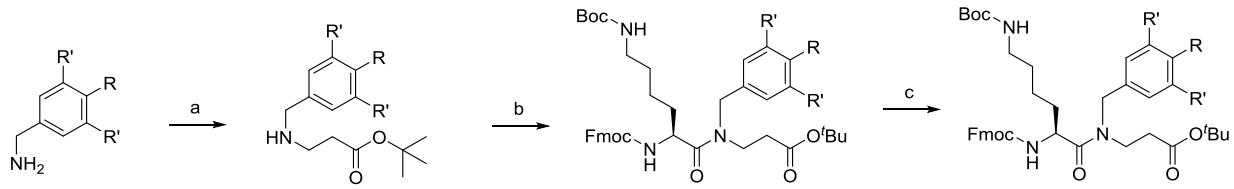
The lipidated peptidomimetic F2M2, Lau-[(*S*)-Aoc]-(Lys-βNphe)$_6$-NH$_2$, is a potent cross-species FPR2 agonist activating human and murine neutrophil NADPH-oxidase

André Holdfeldt[a], Sarah Line Skovbakke[b], Malene Winther[a], Michael Gabl[a], Christina Nielsen[b], Iris Perez-Gassol[b] and Camilla Josephine Larsen[b], Ji Ming Wang[c], Anna Karlsson[a], Claes Dahlgren[a], Huamei Forsman[a,1], Henrik Franzyk[b]

From the [a]Department of Rheumatology and Inflammation Research, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Guldhedsgatan 10A, 413 46 Gothenburg, Sweden, the [b]Department of Drug Design and Pharmacology, Faculty of Health and Medical Sciences, University of Copenhagen, Universitetsparken 2, DK-2100 Copenhagen, Denmark, and the [c]Laboratory of Molecular Immunoregulation, Cancer and Inflammation Program, Frederick National Cancer Institute, Bethesda, Maryland, USA

Materials and general procedures for compound chracterization (HPLC and MS)

Solvents, Rink amide resin, Fmoc-Lys(Boc)-OH, Fmoc-Phe-OH and Fmoc-Aoc-OH and coupling reagents were obtained from IrisBiotech (Marktredwitz, Germany), while octanoic acid, Lau-OSu and Pam-OSu, octanoic acid, decanoic acid, and myristic acid were obtained from Sigma-Aldrich Chemie (Steinheim, Germany). Analytical UHPLC was performed on a Shimadzu Prominence UHPLC system using a Phenomenex Luna C18(2) HTS column (100 × 3.0 mm; particle size: 2.5 μm) eluted at a rate of 0.5 mL/min. Analytical HPLC was performed on a Shimadzu HPLC system with diode array detector (DAD) consisting of an SCL-10A VP controller, an SIL-10AD VP auto injector, an LC-10AT VP Pump, an SPDM10A VP DAD, and a CTO-10AC VP column oven, using a Phenomenex Luna C18(2) column (150 × 4.6 mm; particle size: 3 μm) eluted at a rate of 0.8 mL/min. In both cases injection volumes were 5-10 μL of a ~1 mg/mL solution, and separations were performed at 40 °C. Eluents A (H_2O/MeCN/TFA) 95:5:0.1) and B (MeCN/H_2O/TFA 95:5:0.1) were employed for linear gradient elution (20% B → 100% B during 30 min). Preparative HPLC separations were performed on a Phenomenex Luna C18 (2) column (250 × 21.2 mm; particle size: 5 μm) by using an Agilent 1100 system consisting of two preparative-scale pumps, an autosampler, and a multiple-wavelength UV detector. The eluents A and B were employed with a flow rate of 20 mL/min; injection volumes were 300-900 μL; typically, a linear gradient of 20% B → 80% B during 20 min was employed. High-resolution mass spectra were obtained on a Bruker MicroTOF-Q LC mass spectrometer equipped with an electrospray ionization source and a Quadropole MS detector. The analyses were performed as ESI-MS (m/z): $[M + nH]^{n+}$ for all peptidomimetics.



S1a: R = F; R' = H
S1b: R = R' = F
S1c: R = CF_3; R' = H
S1d: R = CH_3; R' = H

S2a: R = F; R' = H
S2b: R = R' = F
S2c: R = CF_3; R' = H
S2d: R = CH_3; R' = H

S3a: R = F; R' = H
S3b: R = R' = F
S3c: R = CF_3; R' = H
S3d: R = CH_3; R' = H

S4a: R = F; R' = H
S4b: R = R' = F
S4c: R = CF_3; R' = H
S4d: R = CH_3; R' = H

Scheme S1. Synthesis of dimeric building blocks. Reagents and conditions: (a) *tert*-butyl acrylate (0.4 equiv.), 50°C, MeOH, 6 h; (b)

General procedure for the Michael adducts:

To a solution of *tert*-butyl acrylate (25-80 mmol scale) in MeOH (2.5 ml/mmol) in a round-bottomed flask (250 mL) equipped with a condenser was added the appropriate substituted benzylamine (2.5 equiv). The mixture was heated to 50°C (in a silicone oil bath) while stirring for 6 h. The reaction mixture was concentrated and the residue dissolved in DCM (15-40 mL). The solution was loaded onto a VLC column (10 × 10 cm or 8 × 8 cm; packed with silica gel 60H from Merck) pre-treated with heptane. Gradient elution with heptane, heptane–DCM 1:1, DCM and DCM–MeOH 500:1. The fractions containing the Michael adduct were concentrated and dried further on a vacuum line (oil-pump) for 16 h.

Michael adduct **S1a** (4.92 g slightly impure, 24%; 13.27 g, 65%) was prepared as above from 80 mmol *t*-Bu acrylate.
^{1}H NMR (400 MHz), CD_3OD): δ = 1.44 (s, 9 H), 2.45 (t, *J* = 6.9 Hz, 2 H), 2.78 (t, *J* = 6.9 Hz, 2 H), 3.72 (s, 2 H), 7.04 (br t, J = 8.8 Hz, 2 H), 7.34 (dd, *J* = 8.8 and 5.5 Hz, 2 H). ^{13}C NMR (100 Mz, CD_3OD): δ = 28.3, 36.1, 45.2, 53.5, 81.8, 116.1 (d, $^{2}J_{CF}$ = 21.4 Hz), 131.3 (d, $^{3}J_{CF}$ = 8.0 Hz), 136.6 (d, $^{4}J_{CF}$ = 3.3 Hz), 163.5 (d, $^{1}J_{CF}$ = 243.7 Hz), 173.5.

Michael adduct **S1b** (4.86 g, 67%) was prepared as above from 25 mmol *t*-Bu acrylate.
^{1}H NMR (400 MHz), CD_3OD): δ = 1.45 (s, 9 H), 2.44 (t, *J* = 6.8 Hz, 2 H), 2.77 (t, *J* = 6.8 Hz, 2 H), 3.73 (s, 2 H), 7.13 (m, 2 H). ^{13}C NMR (100 Mz, CD_3OD): δ = 28.3, 36.3, 45.2, 53.0, 81.9, 113.3 (dd, $^{2}J_{CF}$ = 17.0 Hz and $^{3}J_{CF}$ = 4.1 Hz), 138.4 (m), 139.8 (dt, $^{1}J_{CF}$ = 248.4 Hz and $^{2}J_{CF}$ = 2 × 15.5 Hz), 152.4 (ddd, $^{1}J_{CF}$ = 247.7 Hz, $^{2}J_{CF}$ = 9.9 Hz, and $^{3}J_{CF}$ = 3.4 Hz), 173.6.

Michael adduct **S1c** (8.82 g, 46%) was prepared as above from 63 mmol *t*-Bu acrylate.
^{1}H NMR (400 MHz), CD_3OD): δ = 1.44 (s, 9 H), 2.46 (t, *J* = 6.8 Hz, 2 H), 2.81 (t, *J* = 6.8 Hz, 2 H), 3.84 (s, 2 H), 7.53 (d, *J* = 8.0 Hz, 2 H), 7.62 (d, *J* = 8.0 Hz, 2 H). ^{13}C NMR (100 Mz, CD_3OD): δ = 28.3, 36.2, 45.4, 53.7, 81.9, 125.8 (q, $^{1}J_{CF}$ = 271.1 Hz), 126.3 (q, $^{3}J_{CF}$ = 3.9 Hz), 129.9, 130.4 (q, $^{2}J_{CF}$ = 32.1 Hz), 145.4, 173.5.

Michael adduct **S1d** (2.65 g slightly impure, 13%; 12.69 g, 63%) was prepared as above from 80 mmol *t*-Bu acrylate.
^{1}H NMR (400 MHz), CD_3OD): δ = 1.43 (s, 9 H), 2.30 (s, 3 H), 2.44 (t, *J* = 6.9 Hz, 2 H), 2.77 (t, *J* = 6.9 Hz, 2 H), 3.68 (s, 2 H), 7.13 (d, *J* = 8.0 Hz, 2 H), 7.19 (d, *J* = 8.0 Hz, 2 H). ^{13}C NMR (100 Mz, CD_3OD): δ = 21.2, 28.3, 36.0, 45.2, 54.0, 81.8, 129.4, 130.1, 137.4, 139.9, 173.5.

General procedure for dimeric building blocks:

In a round-bottomed flask Fmoc-Lys(Boc)-OH (1.1 equiv) was dissolved in DCM (30 mL/g), and then TBTU (1.5 equiv) and DIPEA (2.5 equiv) were added, and the resulting mixture was stirred for 10 min. The Michael adduct was added (17-48 mmol scale; 1 equiv) in DCM (10-20 mL), and then the mixture was stirred for 16 h at room temperature. The reaction mixture was concentrated to ¼ of the volume, diluted with EtOAc (500-1000 mL) and then extracted successively with 1M HCl 1M (250-500 mL, 3×), water (250-500 mL), 0.1M NaOH (250-500 mL, 2×), satd $NaHCO_3$ (250-500 mL), water (250-500 mL), brine (250-500 mL), and finally the organic phase was dried with Na_2SO_4 and then concentrated *in vacuo*. The residue was dissolved in DCM (25-50 mL) and loaded onto a VLC column (8 × 8 cm or 10 × 12 cm; Silica gel 60 from Merck: 15-40 μm) pre-treated with heptane. Gradient elution: heptane followed by heptane–EtOAc 5:1 to 2.5:1. Fractions containing the intermediate *tert*-butyl ester were concentrated and dried on a vacuum line (oil-pump) overnight. An aliquot of this intermediate (12-23 mmol) was treated with TFA–DCM 1:3 (80-160 mL) for 2 h. The mixture was repeatedly co-concentrated with toluene (50 mL, 3×) and then dried on a vacuum line for 1 h. The residue was dissolved in DCM (10 mL/mmol) and then DIPEA (5 equiv) was added (to pH > 8). Then Boc_2O (1.5 equiv) in DCM (2.5 mL/mmol) was added. The mixture was stirred for 16 h. The reaction mixture was concentrated to ¼ volume and was then loaded onto a VLC column (10 × 8 cm, 10 × 9, or 10 × 12 cm; Silica gel 60 from Merck: 15-40 μm) pretreated with heptane. Gradient elution: heptane followed by heptane–EtOAc mixtures (3:1 to 1:1.5) containing 0.1% AcOH. Fractions containing the building blocks were repeatedly co-concentrated with toluene and dried for 16 h on a vacuum line (oil-pump).

Starting from **S2a** (12.27 g; 48.4 mmol) the ester intermediate **S3a** (29.91 g; 88%) was obtained, and an aliquot of this (16.09 g; 22.9 mmol) was converted into Fmoc-Lys(Boc)-βNFphe-OH (**S4a**; 10.88 g, 73%). Analyt. UHPLC: t_R = 5.45 min (50% → 100% B in 10 min; purity: >99.9%).

^{1}H NMR (600 MHz), CD_3OD): δ = 1.21-1.56 (m, 4 H), 1.40* (s, 9H), 1.41 (s, 9 H), 1.63* (m, 2 H), 1.70 (m, 2 H), 2.48 (m, 1 H), 2.57-2.66 (m, 1H), 2.72* (m, 1 H), 2.91-3.08 (m, 2 H), 3.44* (m, 1 H), 3.58-3.75 (m, 2 H), 4.18* (t, *J* = 7.0 Hz, 1H), 4.21 (t, *J* = 6.8 Hz, 1H), 4.29-4.42 (m, 2 H), 4.52-4.65 (m, 3H), 4.78* (d, *J* = 16.8 Hz, 1 H), 7.00 (t, *J* = 8.7 Hz, 1 H), 7.06 (t, 8.7 Hz, 1 H), 7.29-7.35 (m, 4 H), 7.36-7.40 (m, 2 H), 7.63-7.68 (m, 2 H), 7.79 (d, *J* = 7.6 Hz, 2 H).

^{13}C NMR (150 Mz, CD_3OD): δ = 24.0, 24.1*, 28.8, 30.6, 32.8, 32.9, 34.3*, 41.0, 40.9*, 44.0*, 44.1, 48.4, 49.1$^{\#}$, 52.0, 52.5, 52.7*, 67.9, 79.9, 116.6* (d, $^2J_{CF}$ = 21.8 Hz), 116.3 (d, $^2J_{CF}$ = 21.8 Hz), 120.9, 126.2, 128.2**, 128.8, 130.7 (d, $^3J_{CF}$ = 8.1 Hz), 130.2* (d, $^3J_{CF}$ = 8.0 Hz), 134.6 (d, $^4J_{CF}$ = 2.9 Hz), 134.1* (d, $^4J_{CF}$ = 2.1 Hz), 142.6, 145.2*, 145.3, 158.3, 158.4, 163.7* (J = 244.8 Hz), 163.6 (J = 244.3 Hz), 174.6*, 174.8, 175.2, 175.0*.

Starting from **S2b** (4.86 g; 16.8 mmol) the ester intermediate **S3b** (9.48 g; 76%) was obtained, and an aliquot of this (9.00 g; 12.2 mmol) was converted into Fmoc-Lys(Boc)-βNF$_3$phe-OH (**S4b**; 5.36 g; 64%). Analyt. UHPLC: t_R = 6.03 min (50% → 100% B in 10 min; purity: 99.5%).

^{1}H NMR (600 MHz), CD_3OD): δ = 1.26-1.54 (m, 4 H), 1.40* (s, 9H), 1.41 (s, 9 H), 1.58-1.73 (m, 2 H), 2.51* (m, 1 H), 2.59-2.68 (m, 1 H), 2.73 (m, 1 H), 2.94-3.09 (m, 2 H), 3.36* (m, 1 H), 3.62 (m, 1H), 3.70* (m, 1 H), 3.83 (m, 1 H), 4.15* (t, *J* = 6.6 Hz, 1 H), 4.20 (t, *J* = 6.8 Hz, 1H), 4.39-4.46 (m, 2 H), 4.49* (d, *J* = 15.5 Hz, 1H), 4.58-4.64 (m, 3H), 4.80 (d, *J* = 17.5 Hz, 1H), 7.00 (m, 1 H) 7.08-7.15 (m, 2 H), 7.20 (t, *J* = 7.5 Hz, 1 H), 7.26-7.31 (m, 2 H), 7.34-7.38 (m, 2 H), 7.61-7.67 (m, 2 H) 7.77 (d, *J* = 7.5 Hz, 2 H).

^{13}C NMR (150 Mz, CD_3OD): δ = 23.9*, 24.1, 28.8, 30.6, 32.6, 32.9*, 34.4, 40.9*, 41.0, 44.1*, 44.8, 48.4, 49.4, 51.6*, 52.5, 52.8*, 67.9**, 79.9, 112.5* (dd, $^2J_{CF}$ = 17.4 Hz and $^3J_{CF}$ = 3.5 Hz), 112.8 (dd, $^2J_{CF}$ = 17.6 Hz and $^3J_{CF}$ = 4.2 Hz), 120.9, 126.1, 126.3*, 128.7, 128.1*, 128.2, 135.6* (m), 136.0 (m), 139.9 (dt, $^1J_{CF}$ = 249.0 Hz and $^2J_{CF}$ = 2 × 15.4 Hz), 140.1* (dt, $^1J_{CF}$ = 249.6 Hz and $^2J_{CF}$ = 2 × 15.4 Hz), 142.6, 145.3, 145.0*, 145.1, 152.4 (ddd, $^1J_{CF}$ = 248.6 Hz, $^2J_{CF}$ = 9.8 Hz, and $^3J_{CF}$ = 3.2 Hz), 152.6* (ddd, $^1J_{CF}$ = 249.6 Hz, $^2J_{CF}$ = 9.7 Hz, and $^3J_{CF}$ = 2.8 Hz), 158.4*, 158.5, 158.6, 174.5, 174.9*, 175.2, 175.4*.

Starting from **S2c** (8.82 g; 29.1 mmol) the ester intermediate **S3c** (17.01 g; 78%) was obtained, and an aliquot of this (12.56 g; 16.7 mmol) was converted into Fmoc-Lys(Boc)-βNCF$_3$phe-OH (**S4c**; 4.28 g; 37%). Analyt. UHPLC: t_R = 6.29 min (50% → 100% B in 10 min; purity: >99.9%).

^{1}H NMR (600 MHz), CD_3OD): δ = 1.21-1.58 (m, 4 H), 1.40* (s, 9H), 1.41 (s, 9 H), 1.64* (m, 2 H), 1.73 (m, 2 H), 2.52* (m, 1 H), 2.61-2.69 (m, 1 H), 2.73 (m, 1 H), 2.92-3.09 (m, 2 H), 3.44* (m, 1 H), 3.61-3.72 (m, 1 H), 3.79 (m, 1 H), 4.15* (t, *J* = 6.9 Hz, 1 H), 4.21 (t, *J* = 6.9 Hz, 1 H), 4.25-4.33* (m, 2 H), 4.35 (dd, *J* = 10.6 Hz and 6.9 Hz, 1 H), 4.42 (dd, *J* = 10.6 Hz and 6.9 Hz, 1 H), 4.50* (br t, *J* = 6.9 Hz, 1 H), 4.65 (dd, *J* = 8.9 Hz and 4.8 Hz, 1 H), 4.69 (s, 2 H), 4.77* (d, *J* = 17.2 Hz, 1 H), 4.90* (d, *J* = 17.2 Hz, 1 H), 7.10 (t, *J* = 7.3 Hz, 1 H), 7.20 (t, *J* = 7.6 Hz, 1 H), 7.27-7.32 (m, 2 H), 7.35-7.41 (m, 3 H), 7.49* (d, *J* = 7.9 Hz, 1 H), 7.57 (d, *J* = 8.1 Hz, 1 H), 7.62-7.68 (m, 2 H), 7.78 (d, *J* = 7.5 Hz, 2 H).

^{13}C NMR (150 Mz, CD_3OD): δ = 23.0*, 24.1, 28.8**, 30.5, 30.6*, 32.7, 33.0*, 34.4, 41.0, 40.9*, 44.3*, 44.7, 48.4*, 48.5, 49.8, 52.4*, 52.5, 52.7*, 67.9**, 79.8*, 79.9, 120.9, 125.6* (q, $^1J_{CF}$ = 271.2 Hz), 125.7 (q, $^1J_{CF}$ = 270.9 Hz), 126.2, 126.3*, 126.5 (q, $^3J_{CF}$ = 3.3 Hz), 126.8* (q, $^3J_{CF}$ = 3.5 Hz), 128.2**, 128.8, 129.1, 130.5* (q, $^2J_{CF}$ = 32.3 Hz), 130.9 (q, $^2J_{CF}$ = 32.1 Hz), 142.6, 143.0*, 143.3, 145.3, 145.2, 145.1*, 158.4, 158.5*, 158.6, 174.6, 174.9*, 175.3.

Starting from **S2d** (11.94 g; 47.8 mmol) the ester intermediate **S3d** (30.78 g; 92%) was obtained, and an aliquot of this (14.82 g; 21.2 mmol) was converted into Fmoc-Lys(Boc)-βNMephe-OH (**S4d**; 9.18 g; 67%). Analyt. UHPLC: t_R = 5.88 min (50% → 100% B in 10 min; purity: 99.3%).

^{1}H NMR (600 MHz), CD_3OD): δ = 1.20-1.55 (m, 4 H), 1.40 (s, 9H), 1.41* (s, 9 H), 1.60 (m, 2 H), 1.70* (m, 2 H), 2.26 (s, 3 H), 2.27* (s, 3 H), 2.47 (m, 1 H), 2.56-2.65 (m, 1 H), 2.71* (m, 1 H), 2.90-3.08 (m, 2 H), 3.50 (m, 1 H), 3.55-3.64 (m, 1H), 3.70* (m, 1 H), 4.15 (t, *J* = 6.8 Hz, 1 H), 4.20* (t, *J* = 6.8 Hz, 1 H), 4.29-4.35 (m, 2 H), 4.39* (m, 1 H), 4.51*1 (d, *J* = 14.9 Hz, 1 H), 4.57 (t, *J* = 6.8 Hz, 1H), 4.59-4.65 (m, 2 H), 4.74 (d, *J* = 16.6 Hz, 1 H), 7.07-7.22 (m, 4 H), 7.27-7.32 (m, 2 H), 7.36-7.40 (m, 2 H), 7.63-7.68 (m, 2 H), 7.78 (d, *J* = 7.4 Hz, 2 H).

^{13}C NMR (150 Mz, CD_3OD): δ = 21.1**, 24.0, 24.1*, 28.8, 30.5, 30.6*, 33.0, 34.2, 32.9*, 41.0**, 44.0*, 44.2, 48.4**, 49.5*, 52.5*, 52.6, 52.7, 67.9, 68.0*, 79.9, 120.9, 126.2*, 126.3, 128.1, 128.2*, 128.6*, 128.8, 128.9, 130.3, 130.5*, 135.1, 135.5*,138.3*, 138.6, 142.6, 145.3, 145.2*, 158.4, 158.5, 174.6, 174.8, 174.9*, 175.3*.

General procedures for synthesis of peptidomimetics and peptide

The novel α-peptide/β-peptoid peptidomimetics **F2M2-F2M10** and **F2M12-F2M18** were synthesized on a Rink amide resin (loading, 0.5-0.7 mmol/g; 0.05-0.1 mmol scale) in Teflon reactors (10 mL) by standard Fmoc solid-phase synthesis using the appropriate dimeric building blocks. Fmoc deprotection was performed with 20% piperidine in DMF (2 × 10 min, each time with 5 mL; shaking at room temperature). After each Fmoc deprotection and coupling the resin was washed with DMF, MeOH, and DCM (each 3 × 3 min with 5 mL). Coupling of building blocks was performed with PyBOP–DIPEA 1:2 in DMF (2-3 mL DMF; PyBOP: 2.0 equiv for loading, 2.5 equiv for the first two elongations, and 3.0 equiv for subsequent elongations; >2 h under shaking at room temperature). Capping was applied after coupling no. 4 with Ac_2O–DIPEA–NMP 1:2:3 (5 mL, 10 min at room temperature). After the final Fmoc deprotection the N-terminus was acetylated (conditions as for capping) or acylated via coupling of the corresponding acid (5 equiv, 16 h; Fmoc-Aoc-OH, octanoic acid, decanoic acid, or myristic acid) using PyBOP (5 equiv) as coupling reagent, or via coupling with the N-hydroxysuccinimidyl esters (5 equiv, 16 h; Lau-OSu and Pam-OSu; 5 equiv DIPEA). Following cleavage from the resin with TFA–water 95:5 (5 mL, 1 h at room temperature) all peptidomimetics were purified by preparative HPLC. The identity of the compounds was verified by HRMS (ΔM < 10 ppm), and the purity was determined by analytical HPLC (> 95% at 220 nm). After lyophilization target compounds were stored at −20 °C until use.

Peptide **F2M11** was synthesized on a CEM Liberty microwave peptide synthesizer by using Fmoc-based solid-phase peptide synthesis on a Rink Amide AM resin (0.48 mmol/g, 0.1 mmol, 208 mg). Chain elongation was performed by using 0.2 M N^{α}-Fmoc-protected and side chain protected amino acid building blocks (Fmoc-Lys(Boc)-OH and Fmoc-Phe-OH; 5.0 equiv) in DMF in combination with 0.5 M HBTU (5.0 equiv) as coupling reagent and 2 M DIPEA (4.9 Equiv) in NMP as activator base. Fmoc deprotection was performed with 20% piperidine in DMF. Amino acid couplings were conducted at 75°C (25 W for 900 sec), while Fmoc deprotections were conducted at 75°C (37 W for 30 sec followed by 40 W for 180 sec).

Peptidomimetic ***F2M2***. Analytical HPLC (20% → 100% B during 30 min): t_R = 18.98 min (purity: 98.2%). HRMS: calcd for $[M + 3H]^{3+}$ 693.1367, found 693.1367; ΔM = 0.0 ppm.

Peptidomimetic ***F2M3***. Analytical HPLC (20% → 100% B during 30 min): t_R = 16.55 min (purity: 97.5%). HRMS: calcd for $[M + 3H]^{3+}$ 674.4491, found 674.4485 ; ΔM = 0.8 ppm.

Peptidomimetic ***F2M4***. Analytical HPLC (20% → 100% B during 30 min): t_R = 17.88 min (purity: 98.2%). HRMS: calcd for $[M + 3H]^{3+}$ 683.7929, found 683.7949 ; ΔM = 2.9 ppm.

Peptidomimetic ***F2M5***. Analytical HPLC (20% → 100% B during 30 min): t_R = 20.65 min (purity: 98.6%). HRMS: calcd for $[M + 3H]^{3+}$ 702.4804, found 702.4796 ; ΔM = 1.5 ppm.

Peptidomimetic ***F2M6***. Analytical HPLC (20% → 100% B during 30 min): t_R = 22.11 min (purity: 97.2%). HRMS: calcd for $[M + 3H]^{3+}$ 711.8242, found 711.8241; ΔM = 0.1 ppm.

Peptidomimetic ***F2M7***. Analytical HPLC (20% → 100% B during 30 min): t_R = 18.02 min (purity: 97.8%). HRMS: calcd for $[M + 3H]^{3+}$ 683.7929, found 683.7949 ; ΔM = 2.9 ppm.

Peptidomimetic ***F2M8***. Analytical HPLC (20% → 100% B during 30 min): t_R = 20.32 min (purity: 97.0%). HRMS: calcd for $[M + 3H]^{3+}$ 702..4804, found 702.4815 ; ΔM = 1.5 ppm.

Peptidomimetic ***F2M9***. Analytical HPLC (20% → 100% B during 30 min): t_R = 21.82 min (purity: 98.7%). HRMS: calcd for $[M +3H]^{+}$ 711.8242, found 711.8247; ΔM = 0.7 ppm.

Peptidomimetic ***F2M10***. Analytical HPLC (20% → 100% B during 30 min): t_R = 18.98 min (purity: 98.3%). HRMS: calcd for $[M + 3H]^{3+}$ 693.1367, found 693.1356 ; ΔM = 1.5 ppm.

Peptide ***F2M11***. Analytical HPLC (20% → 100% B during 30 min): t_R = 19.30 min (purity: 97.1%). HRMS: calcd for $[M + 3H]^{3+}$ 665.1054, found 665.1034 ; ΔM = 3.0 ppm.

Peptidomimetic ***F2M12***. Analytical HPLC (20% → 100% B during 30 min): t_R = 21.77 min (purity: 98.8%). HRMS: calcd for $[M + 3H]^{3+}$ 801.0801, found 801.0835 ; ΔM = 4.2 ppm.

Peptidomimetic ***F2M13***. Analytical HPLC (20% → 100% B during 30 min): t_R = 19.75 min (purity: 97.7%). HRMS: calcd for $[M + 3H]^{3+}$ 729.1178, found 729.1210 ; ΔM = 4.3 ppm.

Peptidomimetic ***F2M14***. Analytical HPLC (20% → 100% B during 30 min): t_R = 20.61 min (purity: 97.8%). HRMS: calcd for $[M + 3H]^{3+}$ 721.1678, found 721.1668 ; ΔM = 1.3 ppm.

Peptidomimetic ***F2M15***. Analytical HPLC (20% → 100% B during 30 min): t_R = 15.68 min (purity: 98.1%). HRMS: calcd for $[M + 3H]^{3+}$ 693.4563, found 693.4551 ; ΔM = 1.7 ppm.

Peptidomimetic ***F2M16***. Analytical HPLC (20% → 100% B during 30 min): t_R = 13.80 min (purity: 98.5%). HRMS: calcd for $[M + 3H]^{3+}$ 646.4178, found 646.4169 ; ΔM = 1.3 ppm.

Peptidomimetic ***F2M17***. Analytical HPLC (20% → 100% B during 30 min): t_R = 16.67 min (purity: 98.5%). HRMS: calcd for $[M + 3H]^{3+}$ 646.0982, found 646.0964 ; ΔM = 2.7 ppm.