Supplementary Material

Synthesis and optimization of stapled DOCK peptides with improved drug-like properties

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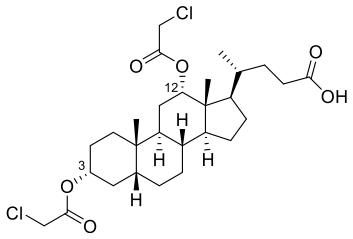
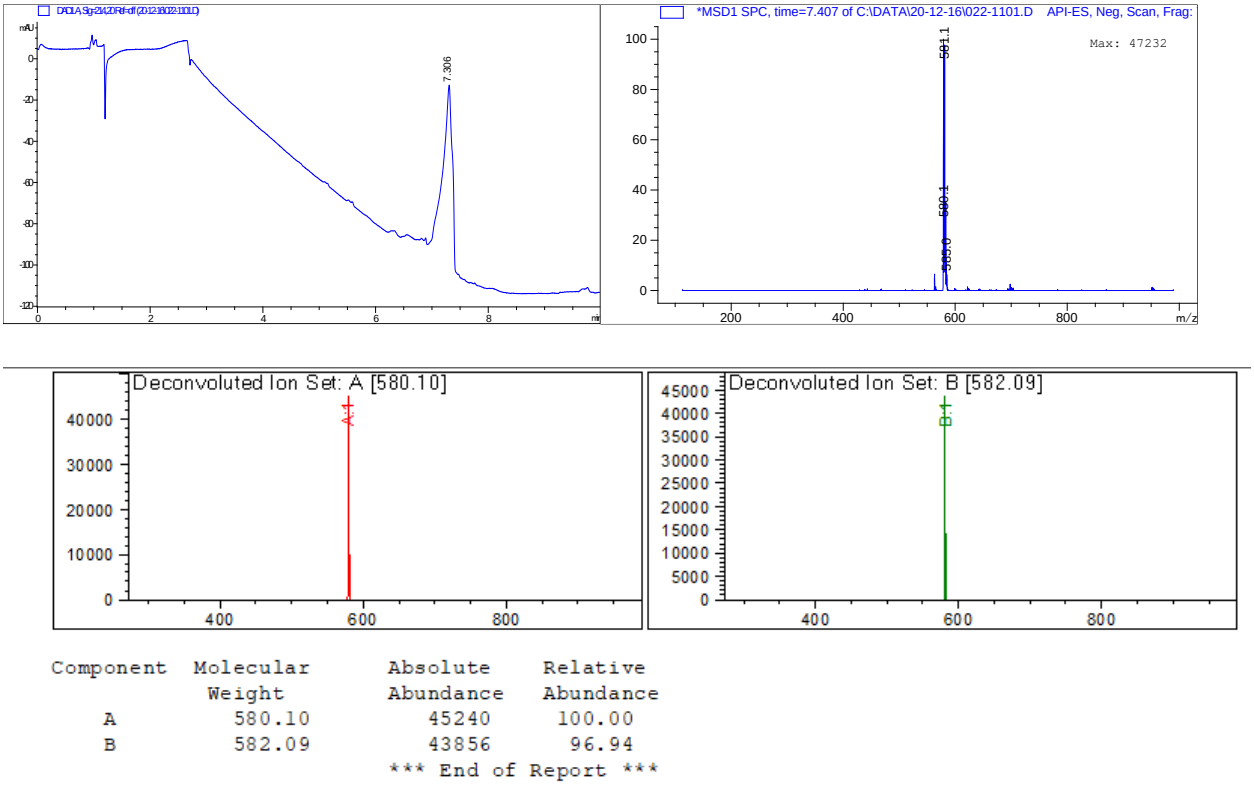
I. Deoxycholic acid derivative characterization (LCMS and NMR)



Chemical Formula: $C_{28}H_{42}Cl_2O_6$
Molecular Weight: 545.5380

LCMS data



Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	580.10	45240	100.00
B	582.09	43856	96.94

*** End of Report ***

Figure S1. LCMS (ESI-MS, negative mode) of deoxycholic acid derivative (C3/C12), found [M + $^{35}Cl]^-$, *m/z* 580.10 and [M + $^{37}Cl]^-$, *m/z* 582.09

^{1}H-NMR data

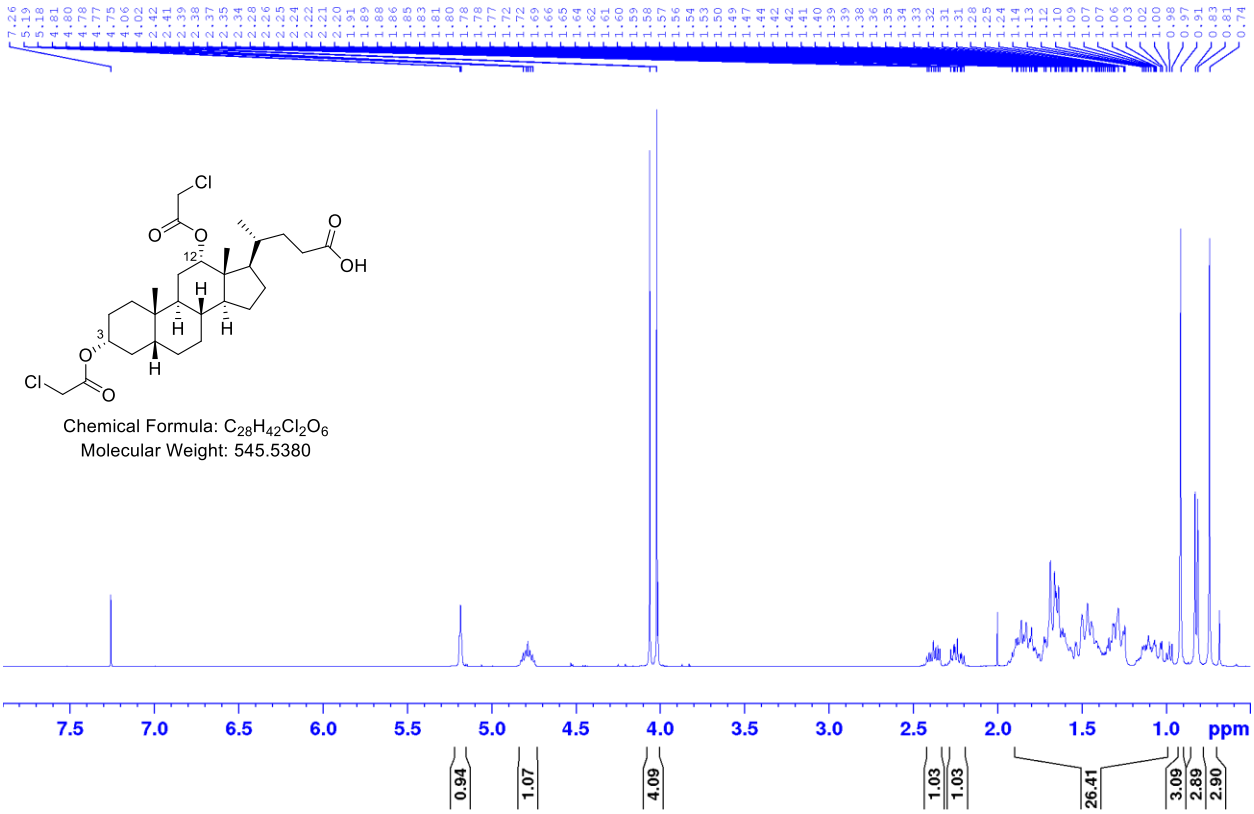


Figure S2. ^{1}H-NMR (400 MHz) of deoxycholic acid derivative (C3/C12) in deuterated chloroform ($CDCl_3$)

II. Liquid Chromatography-Electrospray ionization-Mass Spectrometry (LC-ESI-MS) analysis of peptides

LC-MS analyses were conducted on an Agilent 1100 Series HPLC instrument with diode array detector (DAD), equipped with a Phenomenex Kinetex® EVO/Phenomenex Kinetex C18® 100 Å (150 x 4.6 mm, 5 µm, at 35°C), hyphenated to an Agilent ESI-single quadrupole MS detector type VL. Mass detection operated in either the positive mode or negative mode. A two-solvent system was used: 0.1% formic acid in miliQ water (A) and acetonitrile (B), using a gradient from 0% to 100% B for 15 minutes at a flow rate of 1.5 mL/min at 35 °C.

Table S1. Overview of TATDOCK peptide information and retention times (t_R) *via* LCMS analysis

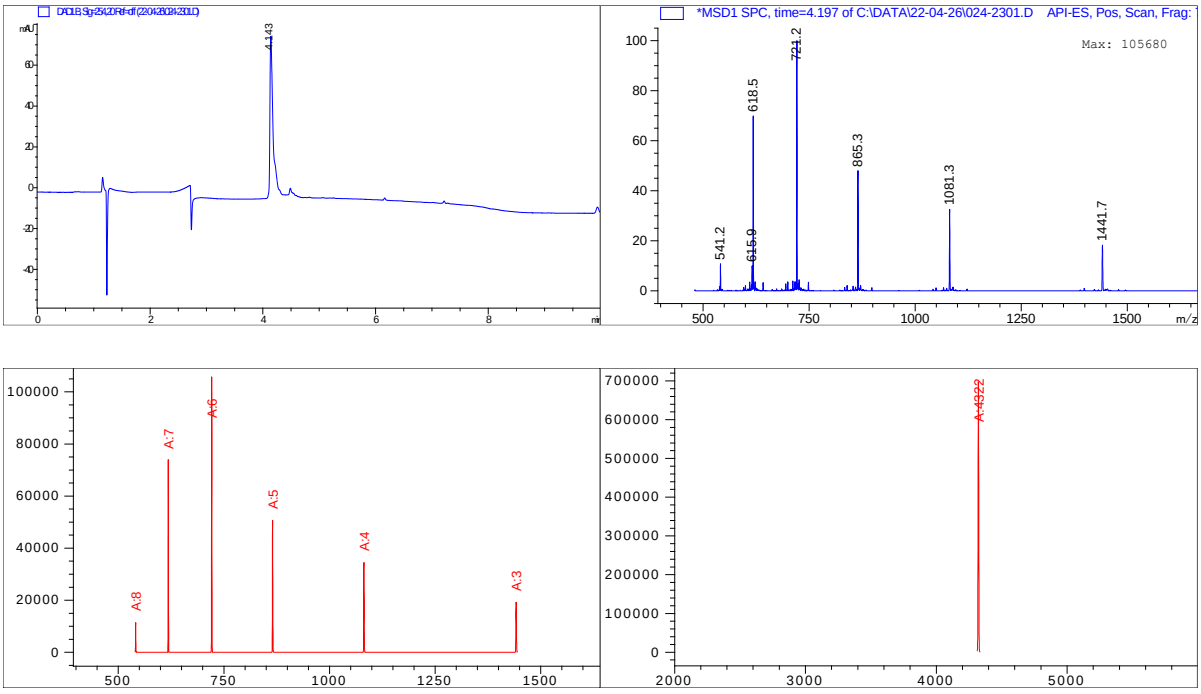
Code	Sequence	Chemical Formula	Exact mass	Retention time (t_R min)
TDWT	GRKKRRQRRRPQPLAQEVTTTLWEW GSIWKQLYVA-NH_2	$C_{195}H_{314}N_{64}O_{48}$	4320.41	4.14
TD-i7	GRKKRRQRRRPQPLAQEVTTTLWEC GSIWKQCYVA-NH_2	$C_{184}H_{303}N_{63}O_{48}S_2$	4227.26	3.94
TD-i7 (S-S)	GRKKRRQRRRPQPLAQEVTTTLWEC* GSIWKQC*YVA-NH_2, *S-S bridge	$C_{184}H_{301}N_{63}O_{48}S_2$	4225.25	3.73
TD-i7-DCA	GRKKRRQRRRPQPLAQEVTTTLWEC* GSIWKQ C*YVA-NH_2, * DCA	$C_{212}H_{343}N_{63}O_{54}S_2$	4699.55	4.28
TD-i7-BP	GRKKRRQRRRPQPLAQEVTTTLWEC* GSIWKQ C*YVA-NH2, * biphenyl (BP)	$C_{198}H_{313}N_{63}O_{48}S_2$	4405.34	4.11
TD-i7-X	GRKKRRQRRRPQPLAQEVTTTLWEC* GSIWKQ C*YVA-NH_2: * m-xylyl (X)	$C_{192}H_{309}N_{63}O_{48}S_2$	4329.31	3.90
TD-i4	GRKKRRQRRRPQPLAQEVTTTLWCW GSCWKQLYVA-NH_2	$C_{190}H_{306}N_{64}O_{46}S_2$	4284.30	4.03
TD-i4-DCA	GRKKRRQRRRPQPLAQEVTTTLWC* WGSC*WKQLYVA-NH_2, * DCA	$C_{218}H_{346}N_{64}O_{52}S_2$	4756.58	4.41
TD-i4-BP	GRKKRRQRRRPQPLAQEVTTTLWC* WGSC*WKQLYVA-NH_2, * biphenyl (BP)	$C_{204}H_{316}N_{64}O_{46}S_2$	4462.38	4.13
TD-i4-X	GRKKRRQRRRPQPLAQEVTTTLWC* WGSC*WKQLYVA-NH_2, * m-xylyl (X)	$C_{198}H_{312}N_{64}O_{46}S_2$	4386.35	4.18
TSWT	GRKKRRQRRRPQEGWASYWLKLAQ WPTTQIVLVET-NH_2	$C_{195}H_{314}N_{64}O_{48}$	4320.41	4.12
TS-i7	GRKKRRQRRRPQEGWASYWLKLAQC *PTTQIVC*VET-NH_2	$C_{184}H_{303}N_{63}O_{48}S_2$	4227.26	3.27
TS-i7-DCA	GRKKRRQRRRPQEGWASYWLKLAQC *PTTQIVC*VET-NH_2, * DCA	$C_{212}H_{343}N_{63}O_{54}S_2$	4699.55	4.21
TS-i7-BP	GRKKRRQRRRPQEGWASYWLKLAQC *PTTQIVC*VET-NH_2, * biphenyl (BP)	$C_{198}H_{313}N_{63}O_{48}S_2$	4405.34	3.96
TS-i7-X	GRKKRRQRRRPQEGWASYWLKLAQC *PTTQIVC*VET-NH_2* m-xylyl (X)	$C_{192}H_{309}N_{63}O_{48}S_2$	4329.31	3.83

Note: LCMS conditions 0-100% MeCN, TD = TATDOCK, WT = wild type, TS = TATDOCK-scrambled, i7 = i,i+7, i4 = i,i+4

II.1 LCMS data of non-modified peptides

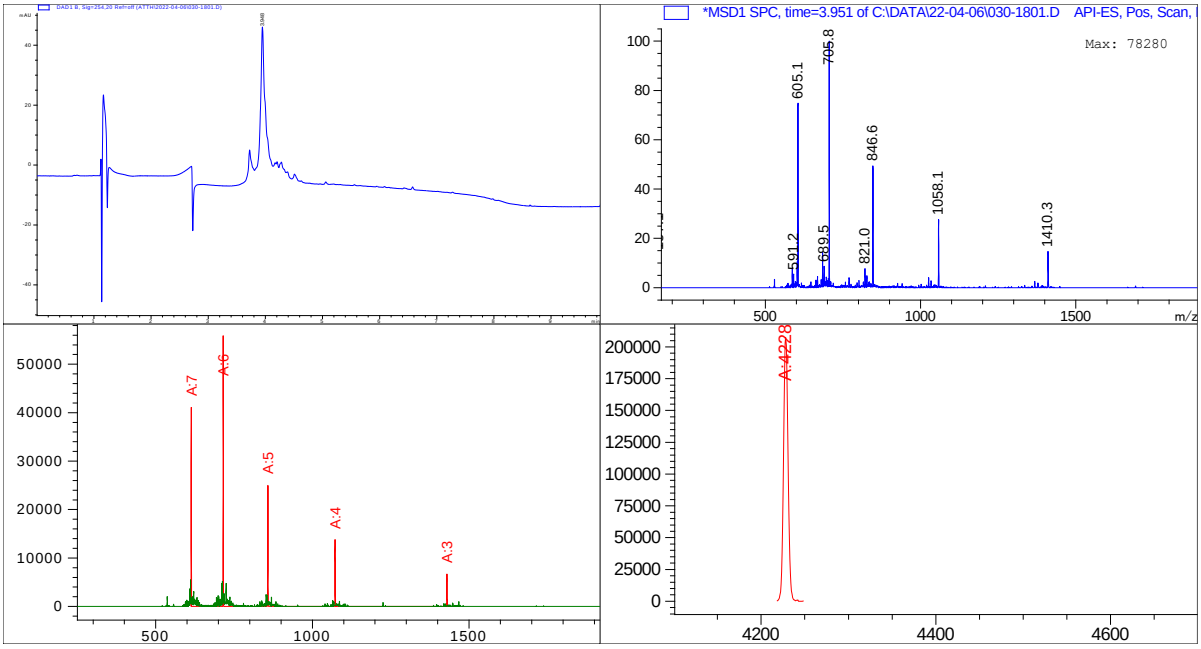
TATDOCK WT (TDWT)

Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWEWGSIWKQLYVA-NH_2
Code	TDWT
Exact mass	4320.41
LCMS (deconvoluted mass)	1441.5 $[M+3H]^{3+}$, 1081.5 $[M+4H]^{4+}$, 865.3 $[M+5H]^{5+}$, 721.3 $[M+6H]^{6+}$, 618.5 $[M+7H]^{7+}$ 541.2 $[M+8H]^{8+}$.

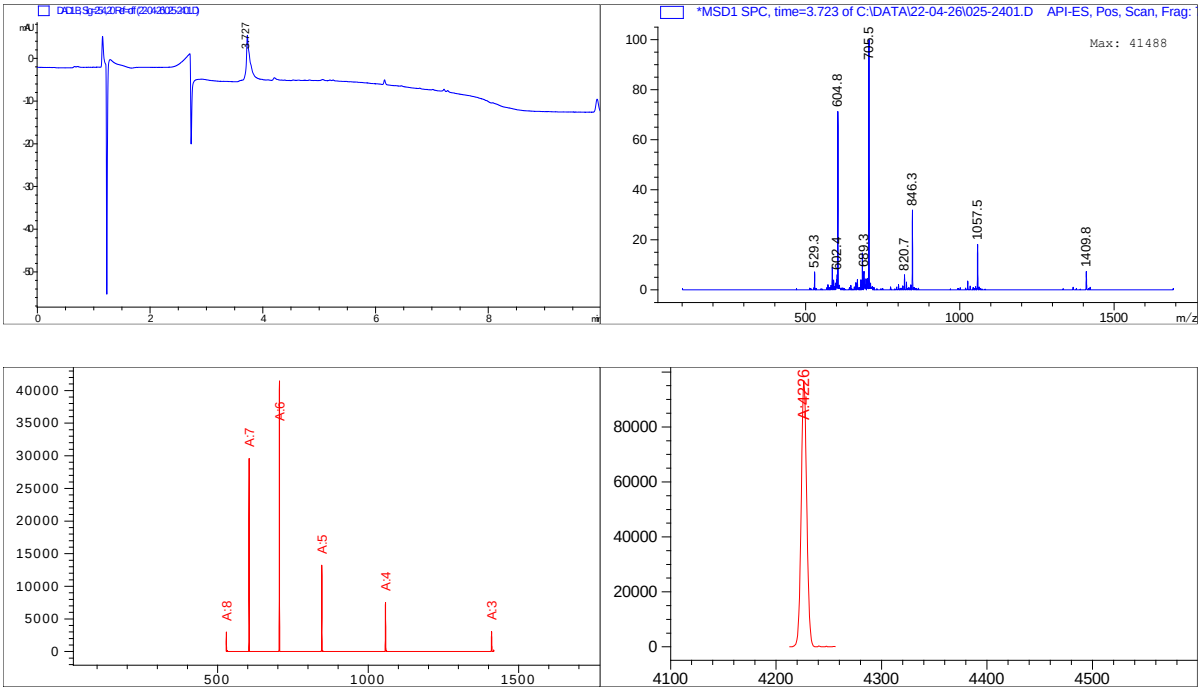


TATDOCK (i,i+7) series (TD-i7)

Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWECGSIWKQCYVA-NH_2
Code	TD (i,i+7)
Exact mass	4227.26
LCMS (deconvoluted mass)	1410.3 $[M+3H]^{3+}$, 1058.1 $[M+4H]^{4+}$, 846.6 $[M+5H]^{5+}$, 705.8 $[M+6H]^{6+}$, 605.1 $[M+7H]^{7+}$.

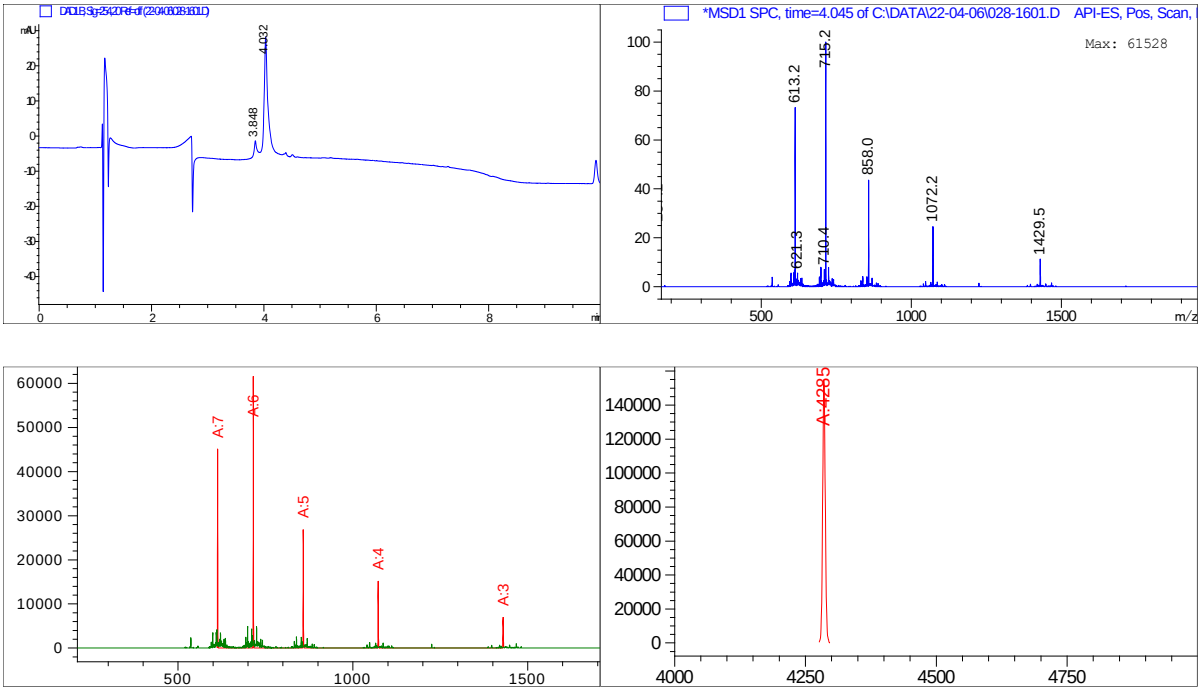


Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWEC(*)GSIWKQC(*)YVA-NH_2 : Disulfide
Code	TD (i,i+7) Di-S-S
Exact mass	4225.25
LCMS (deconvoluted mass)	1409.8 $[M+3H]^{3+}$, 1057.5 $[M+4H]^{4+}$, 846.3 $[M+5H]^{5+}$, 705.5 $[M+6H]^{6+}$, 604.8 $[M+7H]^{7+}$, 529.3 $[M+8H]^{8+}$.



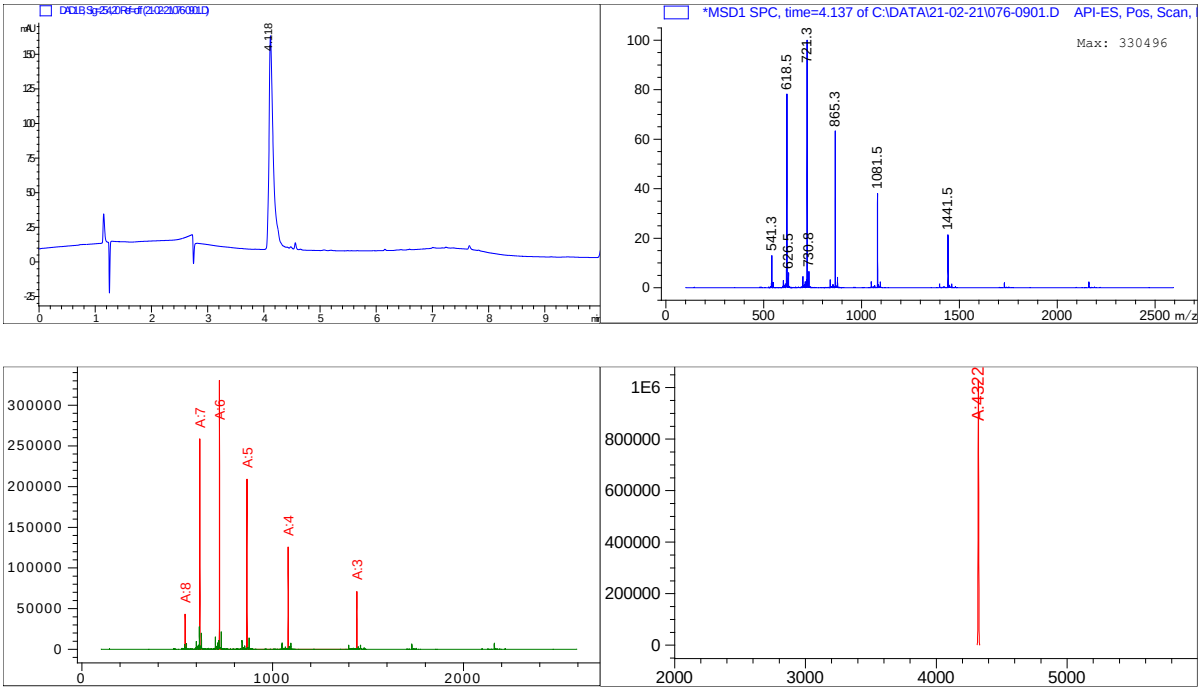
TATDOCK (i,i+4) series (TD-i4)

Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWCWGSCWKQLYVA-NH_2
Code	TD (i,i+4)
Exact mass	4284.30
LCMS (deconvoluted mass)	1429.5 $[M+3H]^{3+}$, 1072.2 $[M+4H]^{4+}$, 858.0 $[M+5H]^{5+}$, 715.2 $[M+6H]^{6+}$, 613.2 $[M+7H]^{7+}$.



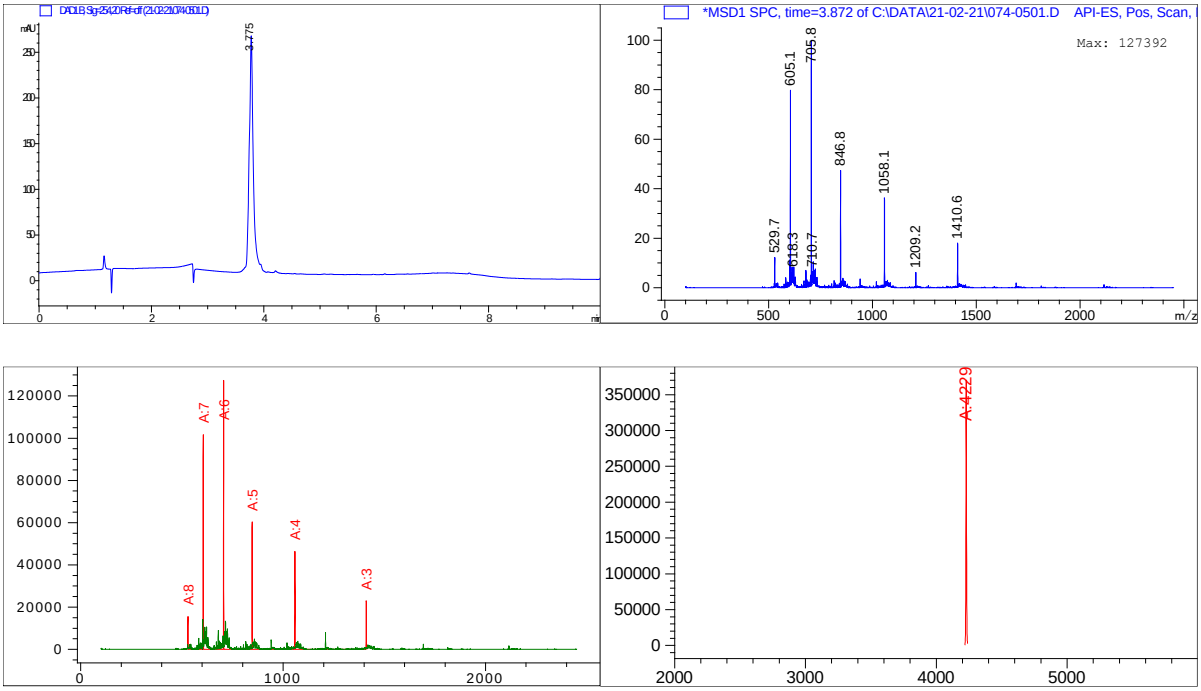
TATDOCK WT scrambled (TSWT)

Peptide	H-GRKKRRQRRRPQEGWASYWLKLAQWPTTQIVLVET-NH_2
Code	TSWT
Exact mass	4320.41
LCMS (deconvoluted mass)	1441.5 $[M+3H]^{3+}$, 1081.5 $[M+4H]^{4+}$, 865.3 $[M+5H]^{5+}$, 721.3 $[M+6H]^{6+}$, 618.5 $[M+7H]^{7+}$, 541.3 $[M+8H]^{8+}$.



TATDOCK (i,i+7) scrambled series (TS-i7)

Peptide	H-GRKKRRQRRRPQEGWASYWLKLAQC(*)PTTQIVC(*)VET-NH_2
Code	TS-i7
Exact mass	4227.26
LCMS (deconvoluted mass)	1410.6 $[M+3H]^{3+}$, 1058.1 $[M+4H]^{4+}$, 846.8 $[M+5H]^{5+}$, 705.8 $[M+6H]^{6+}$, 605.1 $[M+7H]^{7+}$, 529.7 $[M+8H]^{8+}$.



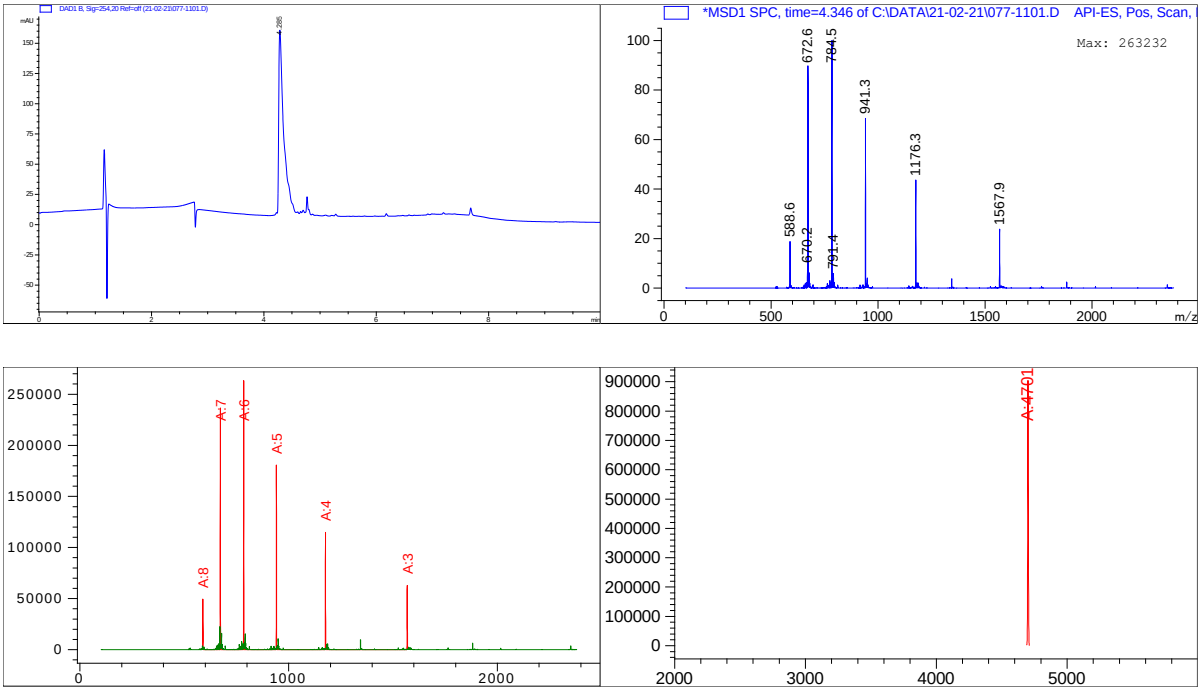
II.2 LCMS data of stapled peptides

Table S2. Yields of stapled peptides after optimization

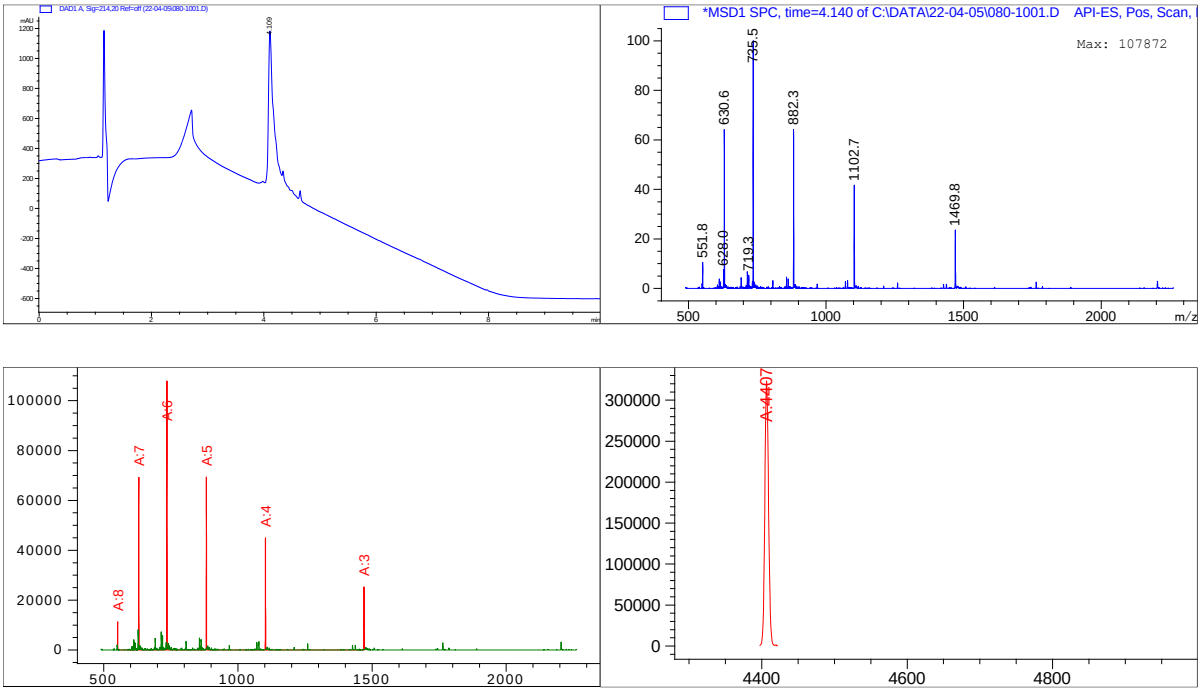
Linear peptide	% Yield		
	DCA	BP	X
TD (*i,i+7*)	53	73	65
TS (*i,i+7*)	86	67	97
TD (*i,i+4*)	38	45	61
DOCK (*i,i+7*)	84	54	-

DCA: deoxycholic acid, BP: biphenyl, X: *m*-xylyl

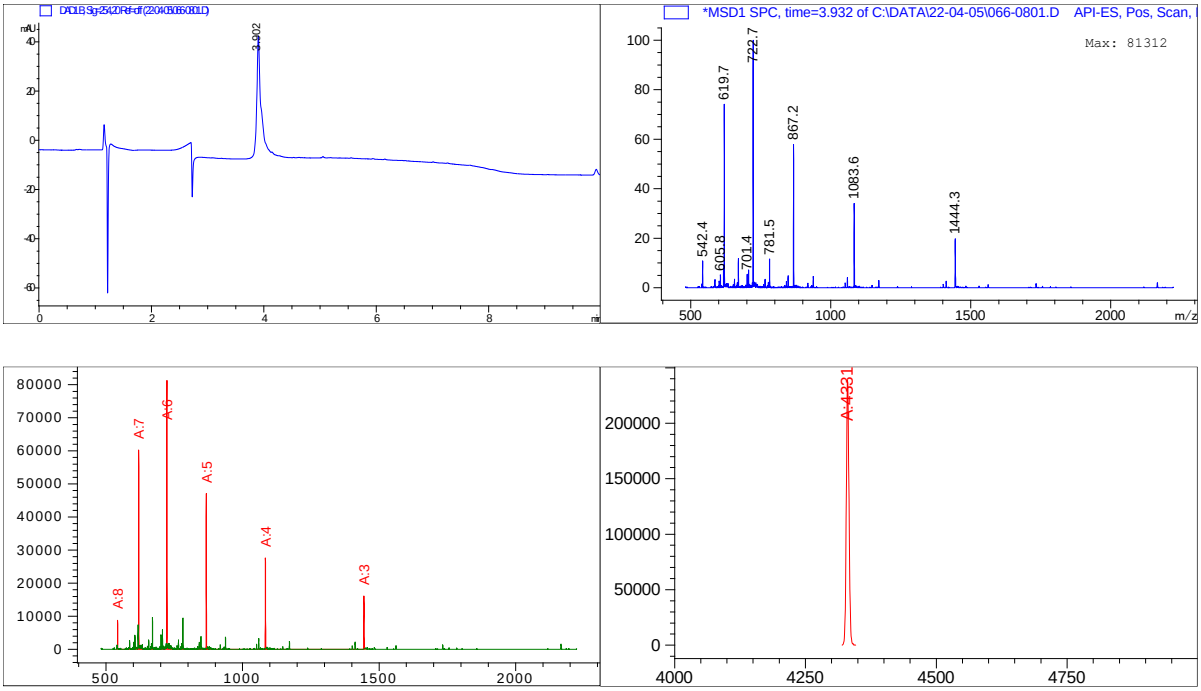
Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWEC(*)GSIWKQ C(*)YVA-NH_2: * DCA
Code	TD (i,i+7) DCA
Exact mass	4699.55
LCMS (deconvoluted mass)	1567.9 $[M+3H]^{3+}$, 1176.3 $[M+4H]^{4+}$, 941.3 $[M+5H]^{5+}$, 784.5 $[M+6H]^{6+}$, 672.6 $[M+7H]^{7+}$ 588.6 $[M+8H]^{8+}$.



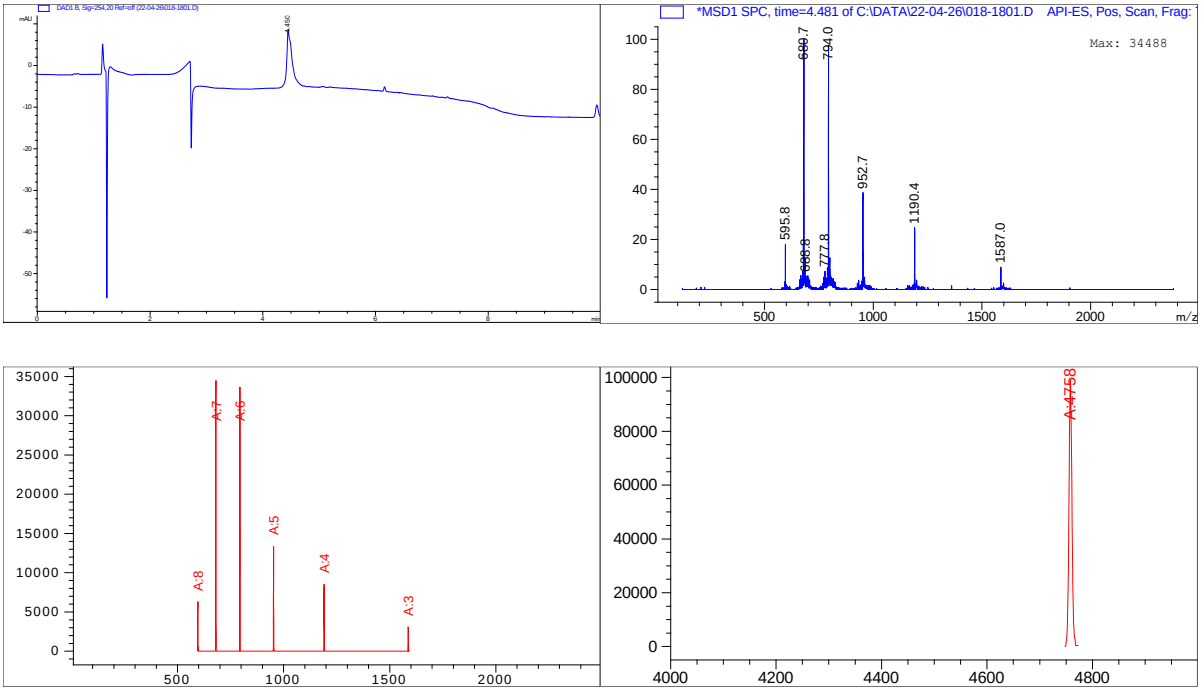
Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWEC(*)GSIWKQ C(*)YVA-NH_2: * biphenyl
Code	TD (i,i+7) BP
Exact mass	4405.34
LCMS (deconvoluted mass)	1469.8 $[M+3H]^{3+}$, 1102.7 $[M+4H]^{4+}$, 882.3 $[M+5H]^{5+}$, 735.5 $[M+6H]^{6+}$, 630.6 $[M+7H]^{7+}$ 551.8 $[M+8H]^{8+}$.



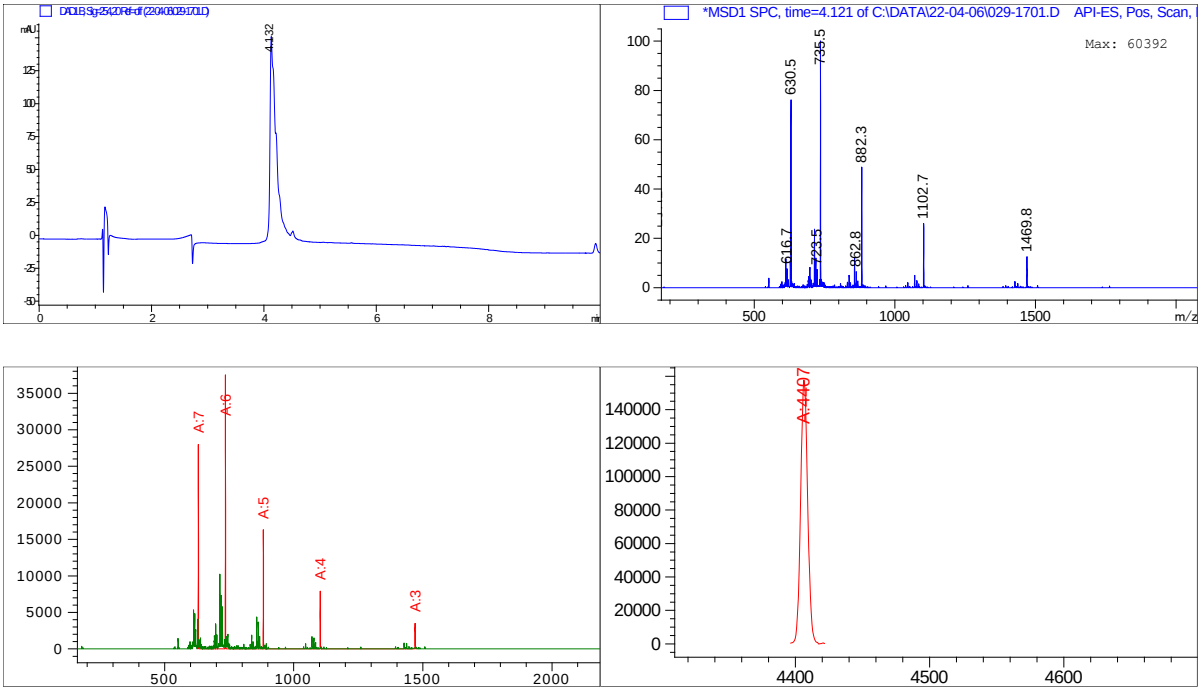
Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWEC(*)GSIWKQ C(*)YVA-NH_2: * *m-xylyl*
Code	TD (i,i+7) X
Exact mass	4329.31
LCMS (deconvoluted mass)	1444.5 $[M+3H]^{3+}$, 1083.6 $[M+4H]^{4+}$, 867.2 $[M+5H]^{5+}$, 722.8 $[M+6H]^{6+}$, 619.7 $[M+7H]^{7+}$ 542.4 $[M+8H]^{8+}$.



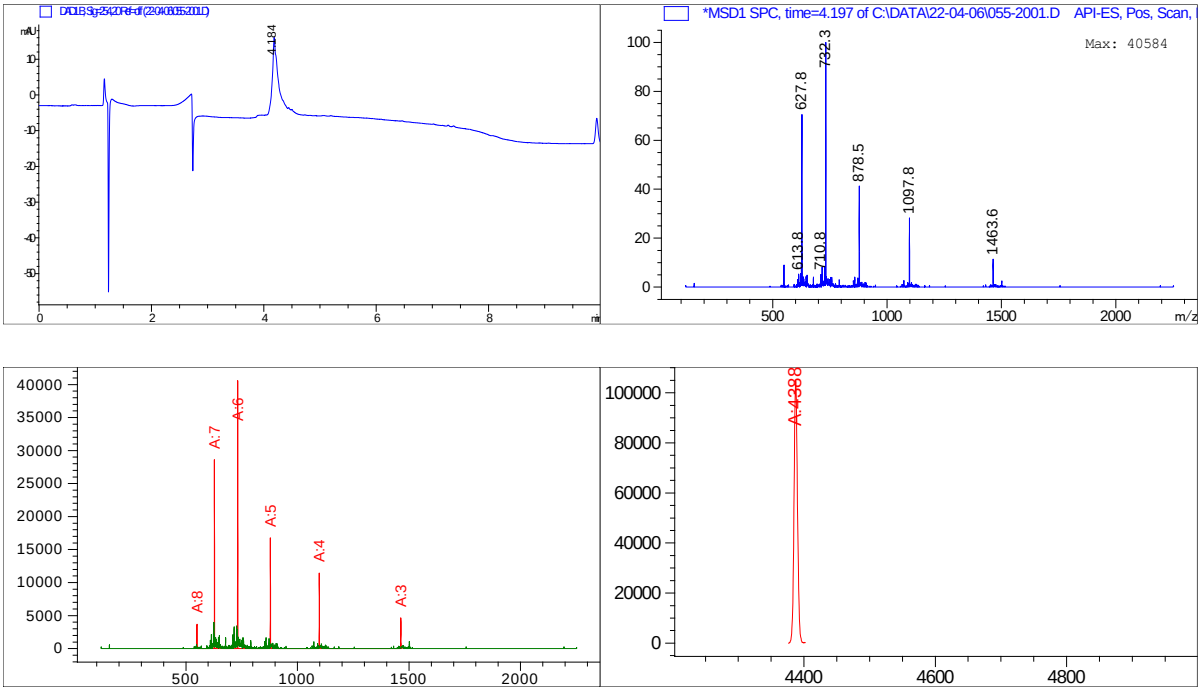
Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWC(*)WGSC(*)WKQLYVA-NH_2: *DCA
Code	TD (i,i+4) DCA
Exact mass	4756.58
LCMS (deconvoluted mass)	1587.0 $[M+3H]^{3+}$, 1190.4 $[M+4H]^{4+}$, 952.7 $[M+5H]^{5+}$, 794.0$[M+6H]^{6+}$, 680.7 $[M+7H]^{7++}$, 595.8 $[M+8H]^{8+}$.



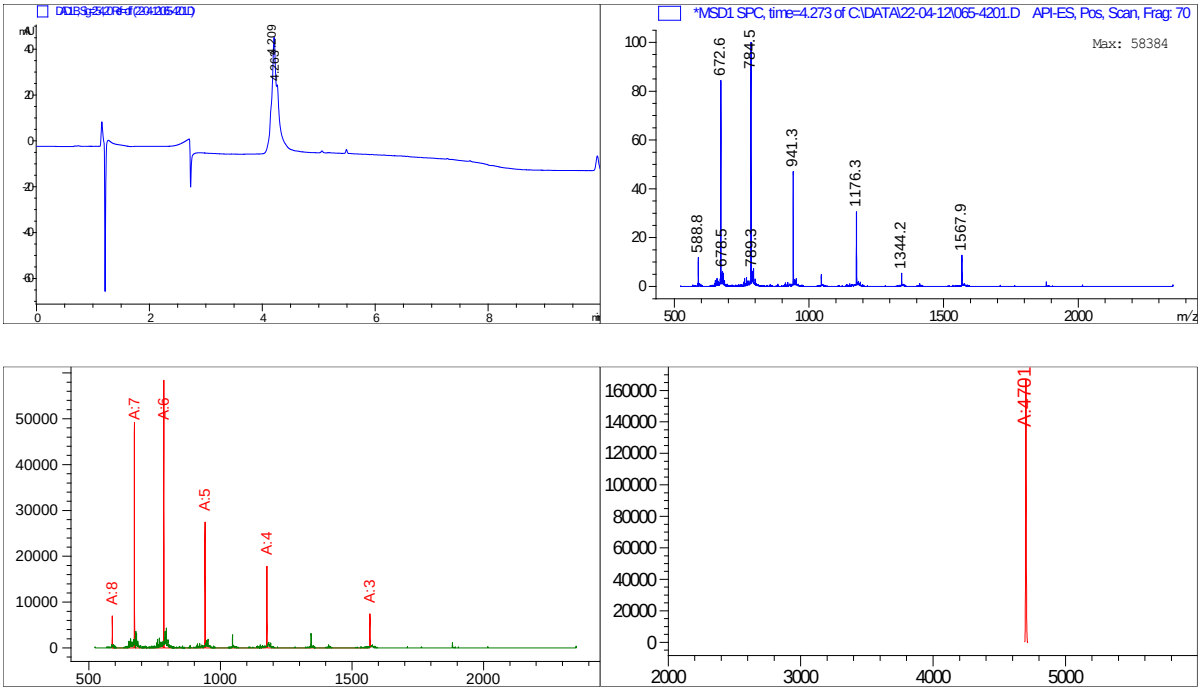
Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWC(*)WGSC(*)WKQLYVA-NH_2: *biphenyl
Code	TD (i,i+4) BP
Exact mass	4462.38
LCMS (deconvoluted mass)	1469.8 $[M+3H]^{3+}$, 1102.7 $[M+4H]^{4+}$, 882.3 $[M+5H]^{5+}$, 735.5 $[M+6H]^{6+}$, 630.5 $[M+7H]^{7+}$.



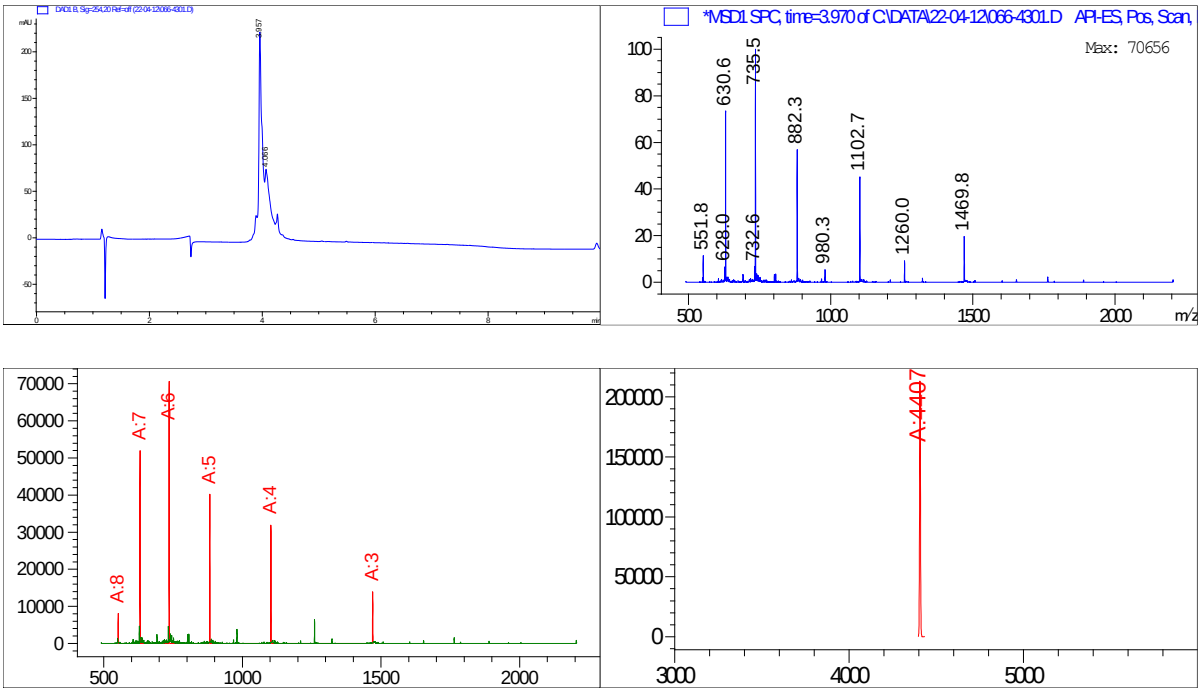
Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWC(*)WGSC(*)WKQLYVA-NH_2: * *m-xylyl*
Code	TD (i,i+4) X
Exact mass	4386.35
LCMS (deconvoluted mass)	1463.6 $[M+3H]^{3+}$, 1097.8 $[M+4H]^{4+}$, 878.5 $[M+5H]^{5+}$, 732.3 $[M+6H]^{6+}$, 627.8 $[M+7H]^{7+}$ 549.5 $[M+8H]^{8+}$.



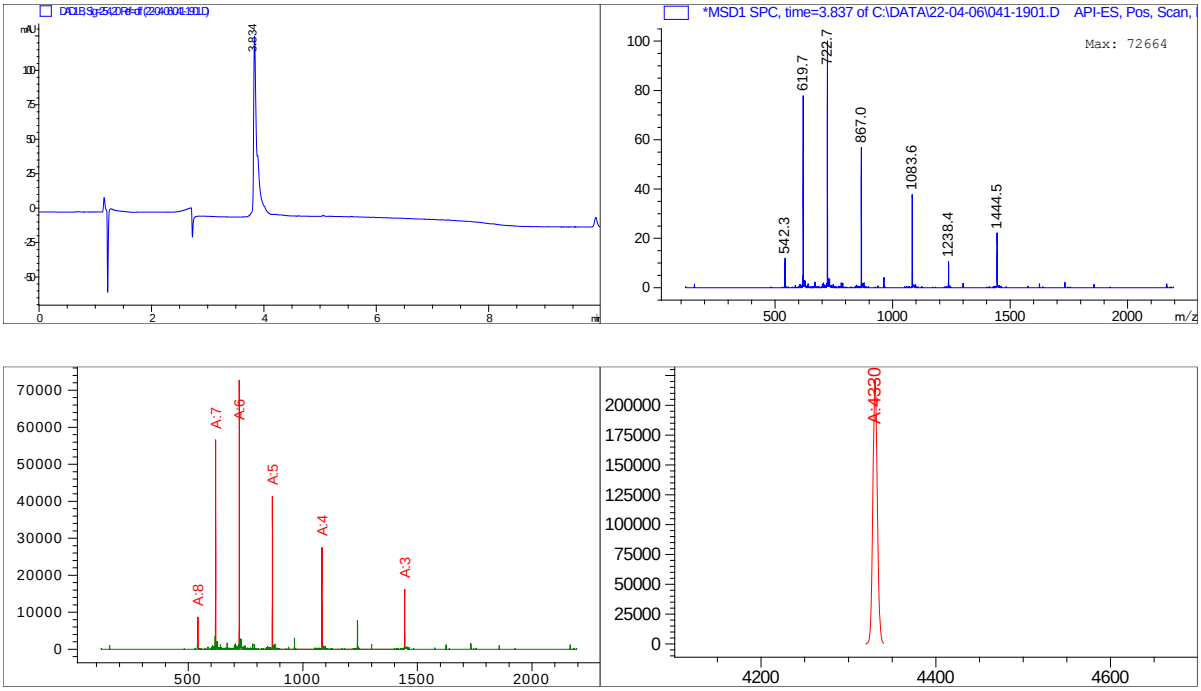
Peptide	H-GRKKRRQRRRPQEGWASYWLKLAQC(*)PTTQIVC(*)VET-NH_2: **DCA*
Code	TS-i7-DCA
Exact mass	4699.55
LCMS (deconvoluted mass)	1567.9 $[M+3H]^{3+}$, 1176.3 $[M+4H]^{4+}$, 941.3 $[M+5H]^{5+}$, 784.5 $[M+6H]^{6+}$, 672.6 $[M+7H]^{7+}$, 588.8 $[M+8H]^{8+}$.



Peptide	H-GRKKRRQRRRPQEGWASYWLKLAQC(*)PTTQIVC(*)VET-NH_2: *biphenyl
Code	TS-i7-BP
Exact mass	4405.34
LCMS (deconvoluted mass)	1469.8 $[M+3H]^{3+}$, 1102.7 $[M+4H]^{4+}$, 882.3 $[M+5H]^{5+}$, 735.5 $[M+6H]^{6+}$, 630.6 $[M+7H]^{7+}$, 551.8 $[M+8H]^{8+}$.



Peptide	H-GRKKRRQRRRPQEGWASYWLKLAQC(*)PTTQIVC(*)VET-NH_2: * *m-xylyl*
Code	TS-i7-X
Exact mass	4329.31
LCMS (deconvoluted mass)	1444.5 $[M+3H]^{3+}$, 1083.6 $[M+4H]^{4+}$, 867.0 $[M+5H]^{5+}$, 722.7 $[M+6H]^{6+}$, 619.7 $[M+7H]^{7+}$, 542.3 $[M+8H]^{8+}$.



II.3 Regioisomer analysis of DCA-stapled peptides

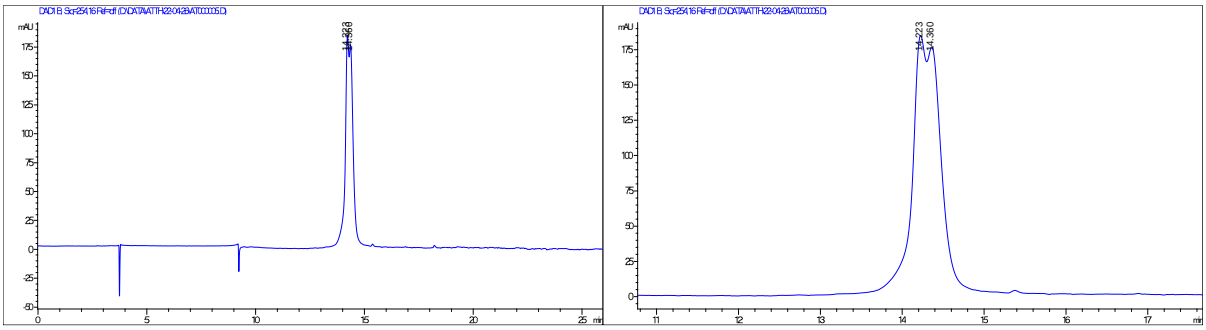


Figure S3. HPLC chromatogram of TATDOCK *(i,i+4)* DCA showing two regioisomers (t_R = 14.22 and 14.36 min at 254 nm) via analytical Luna C18 column (250 x 4.6 mm, 5 µm particle size, 100Å), gradient 0-100% MeCN for 15 min at 35°C

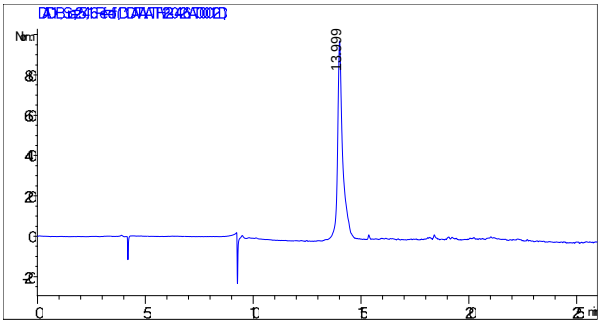
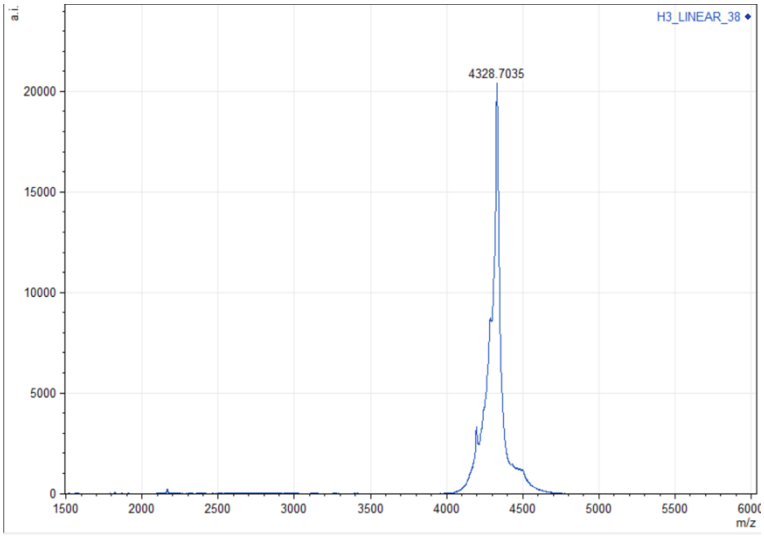


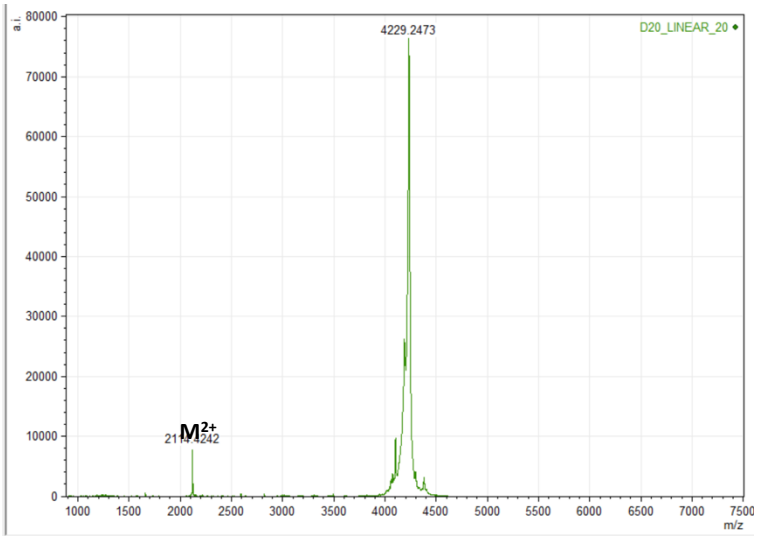
Figure S4. HPLC chromatogram of TATDOCK *(i,i+7)* DCA (t_R = 13.99 min at 254 nm) via analytical Luna C18 column (250 x 4.6 mm, 5 µm particle size,100Å), gradient 0-100% MeCN for 15 min at 35°C

III. MALDI-TOF-MS data

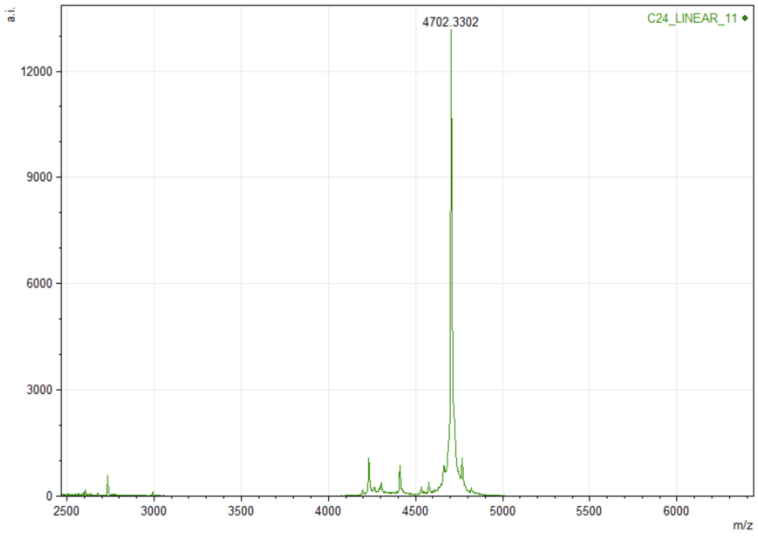
Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWEWGSIWKQLYVA-NH_2
Code	TDWT
MW (g/mole)	4323.06



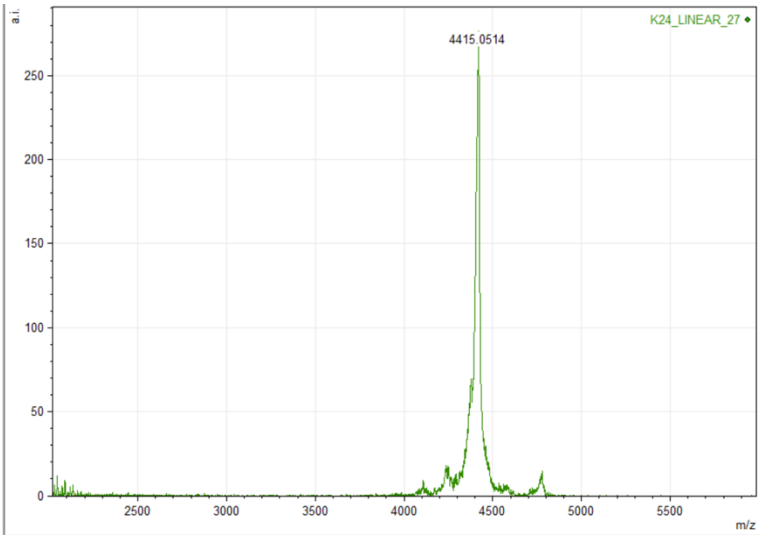
Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWEC(*)GSIWKQ C(*)YVA-NH_2
Code	TD (i,i+7)
MW (g/mole)	4229.96



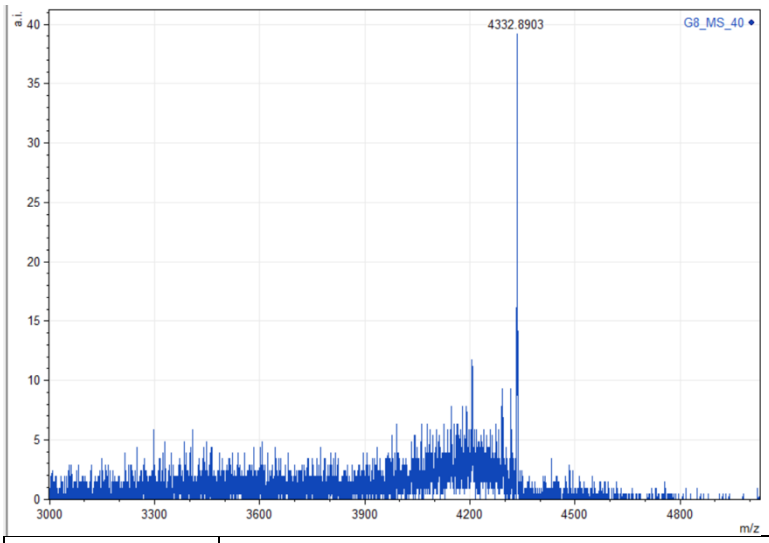
Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWEC(*)GSIWKQ C(*)YVA-NH_2: * DCA
Code	TD (i,i+7) DCA
MW (g/mole)	4702.58



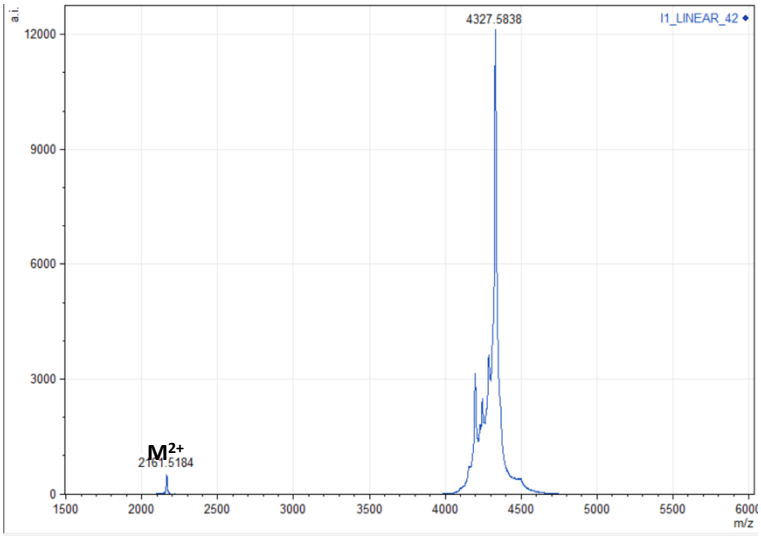
Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWEC(*)GSIWKQ C(*)YVA-NH_2: * biphenyl
Code	TD (i,i+7) BP
MW (g/mole)	4408.20



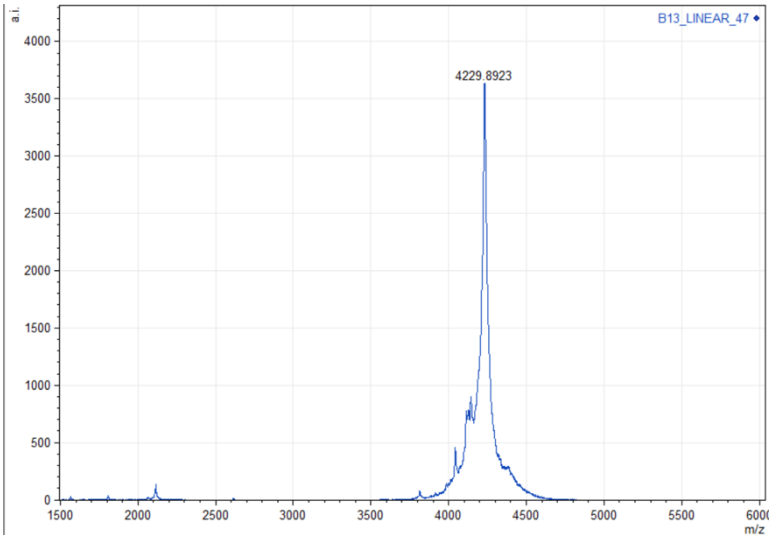
Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWEC(*)GSIWKQ C(*)YVA-NH_2: * *m*-xylyl
Code	TD (i,i+7) X
MW (g/mole)	4332.10



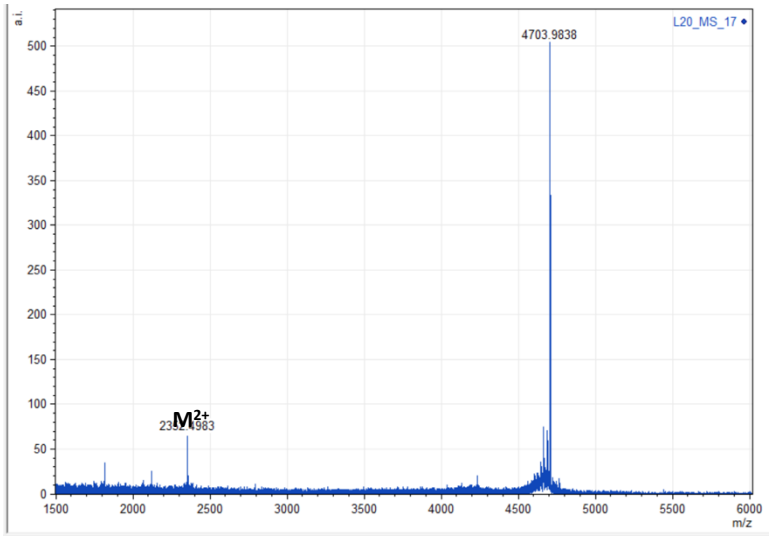
Peptide	H-GRKKRRQRRRPQEGWASYWLKLAQWPTTQIVLVET-NH_2
Code	TSWT
MW (g/mole)	4323.06



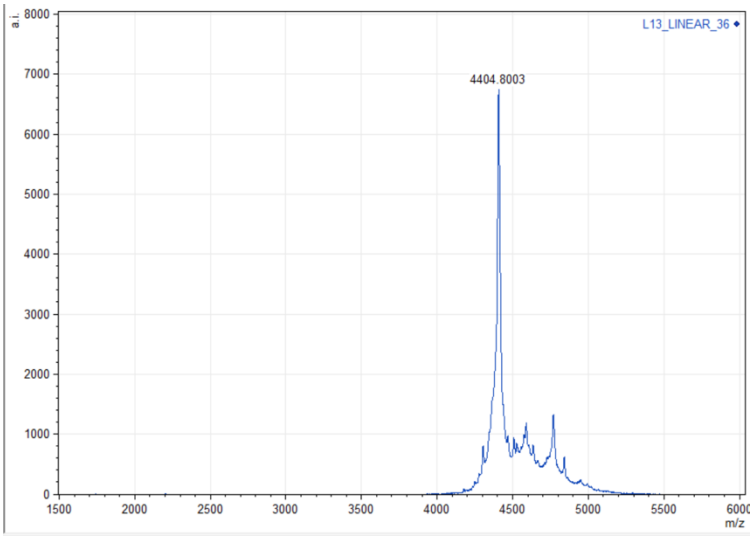
Peptide	H-GRKKRRQRRRPQEGWASYWLKLAQC(*)PTTQIVC(*)VET-NH_2
Code	TS-i7
MW (g/mole)	4229.96



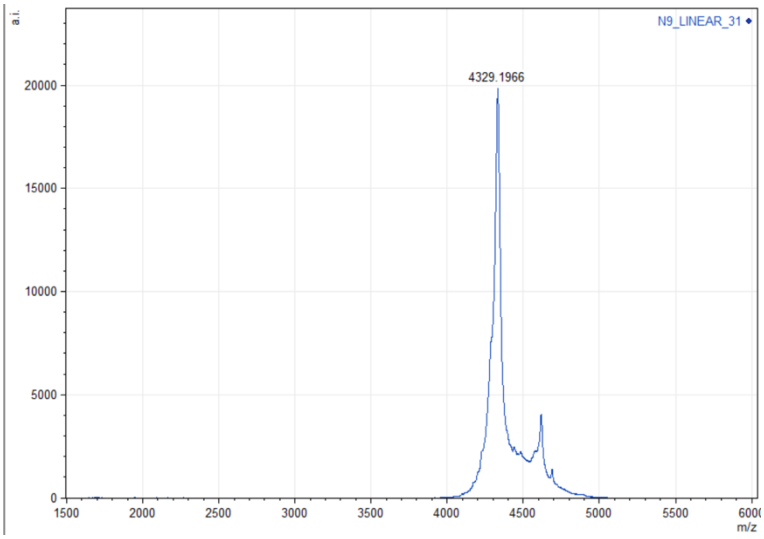
Peptide	H-GRKKRRQRRRPQEGWASYWLKLAQC(*)PTTQIVC(*)VET-NH_2: **DCA*
Code	TS-i7-DCA
MW (g/mole)	4702.58



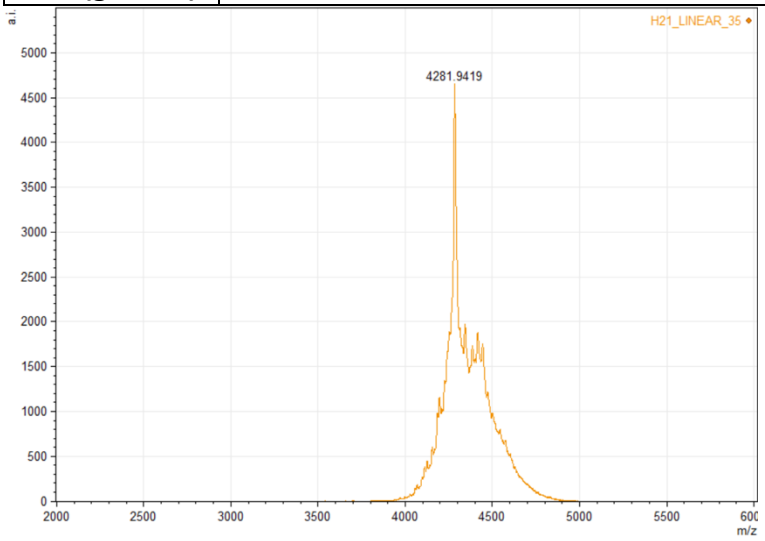
Peptide	H-GRKKRRQRRRPQEGWASYWLKLAQC(*)PTTQIVC(*)VET-NH_2: *biphenyl
Code	TS-i7-BP
MW (g/mole)	4408.20



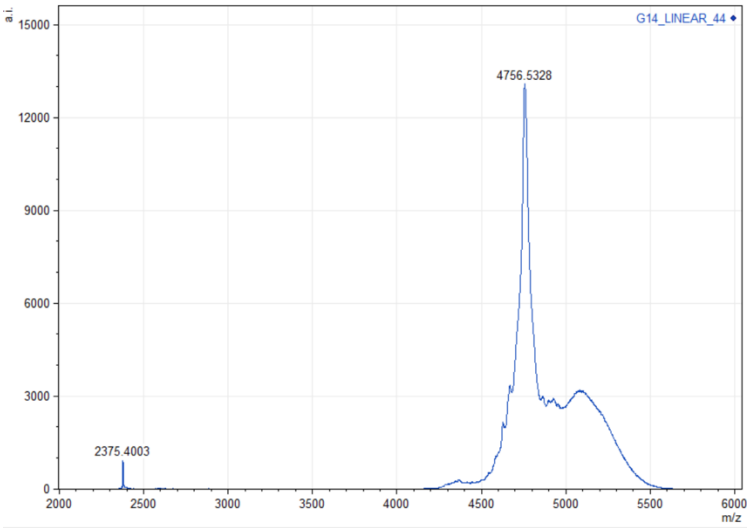
Peptide	H-GRKKRRQRRRPQEGWASYWLKLAQC(*)PTTQIVC(*)VET-NH_2: **m*-xylenyl
Code	TS-i7-X
MW (g/mole)	4332.10



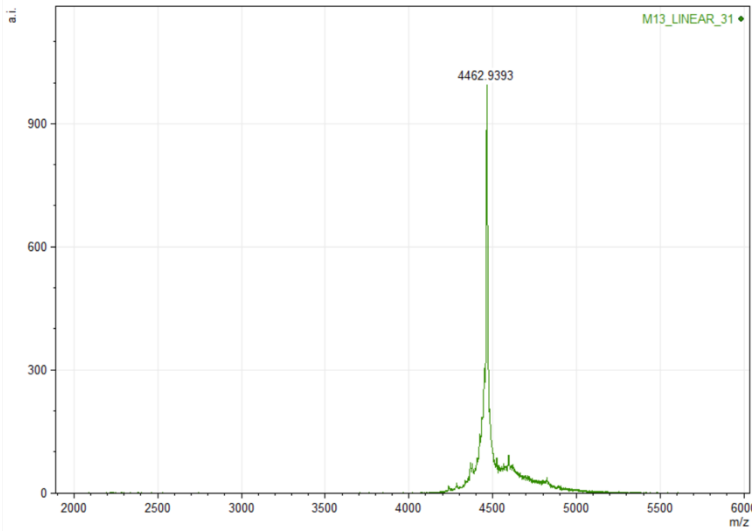
Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWCWGSCWKQLYVA-NH_2
Code	TD (i,i+4)
MW (g/mole)	4287.06



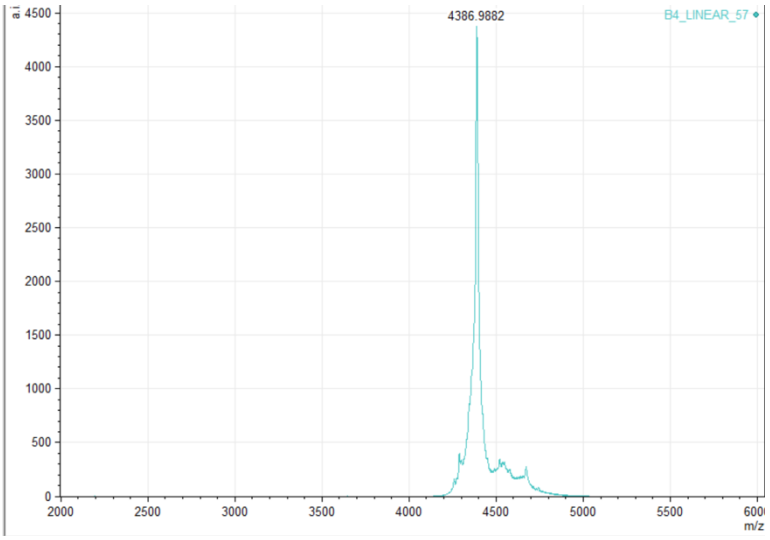
Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWC(*)WGSC(*)WKQLYVA-NH_2: *DCA
Code	TD (i,i+4) DCA
MW (g/mole)	4759.68



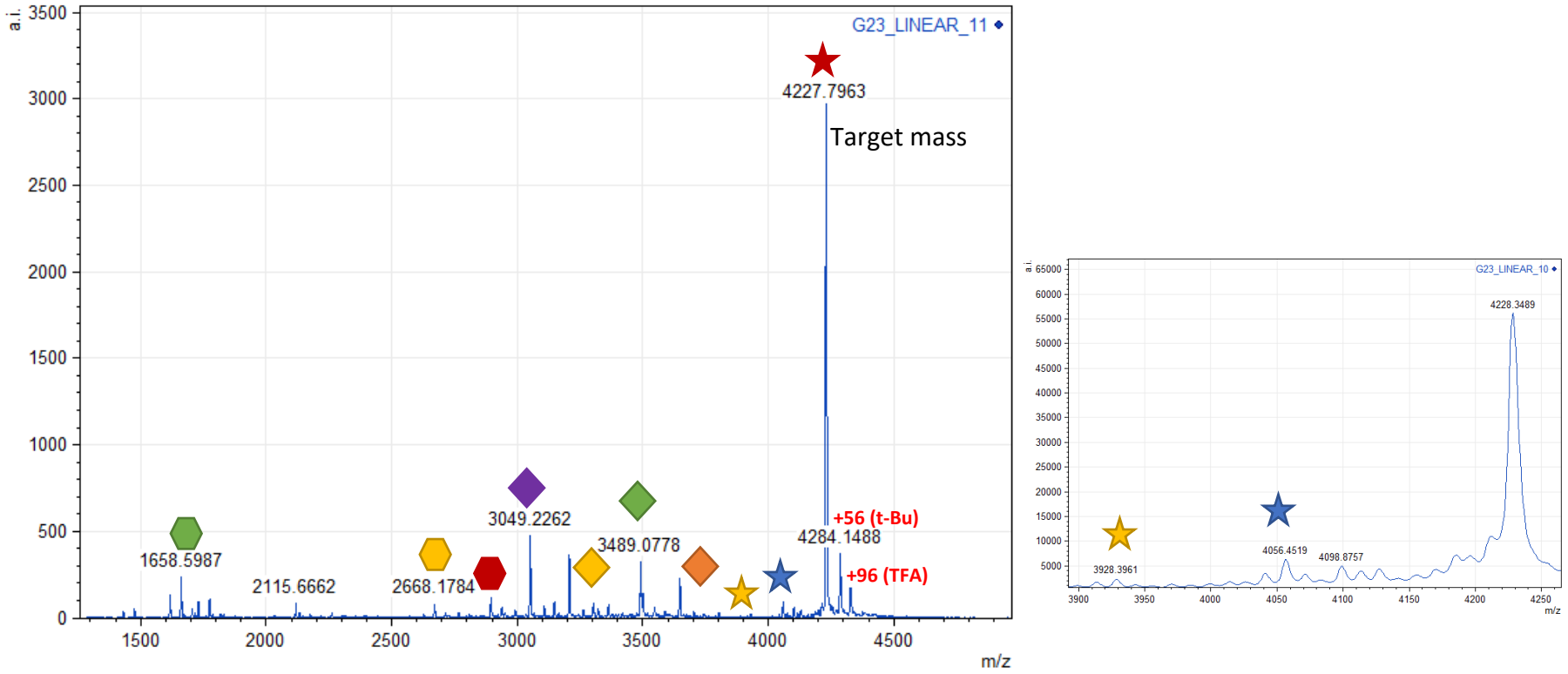
Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWC(*)WGSC(*)WKQLYVA-NH_2: *biphenyl
Code	TD (i,i+4) BP
MW (g/mole)	4465.29

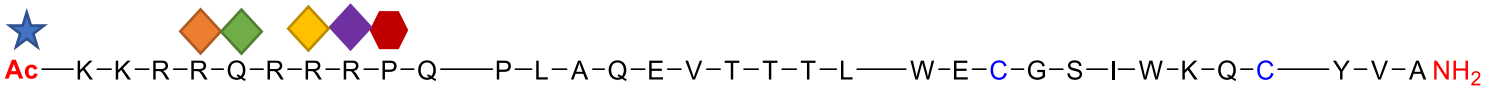


Peptide	H-GRKKRRQRRRPQPLAQEVTTTLWC(*)WGSC(*)WKQLYVA-NH_2: **m*-xylenyl
Code	TD (i,i+4) X
MW (g/mole)	4389.20



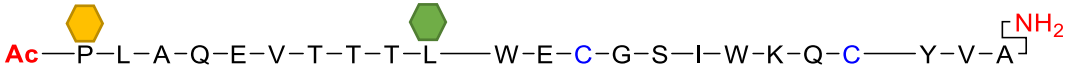
Proposed deletion products during peptide synthesis (SPPS)
Using Fmoc-Rink Amide AM resin





33 residues

Molecular Weight: 4058.76

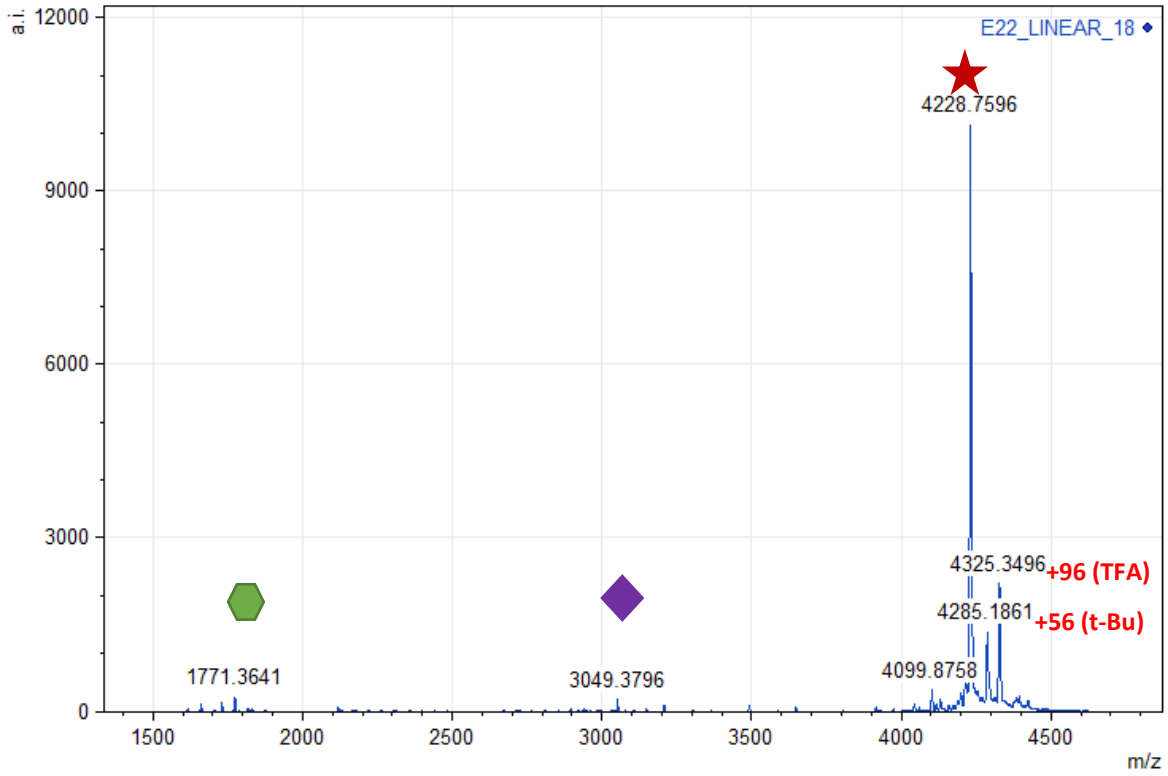


23 residues

Molecular Weight: 2668.08

Figure S5. MALDI-TOF-MS results of crude peptide (TATDOCK *i,i*+7) using Fmoc-Rink Amide AM resin (0.69 mmol/g) under HBTU/DIPEA conditions and proposed mass identification.

Using hemMatrix® resin



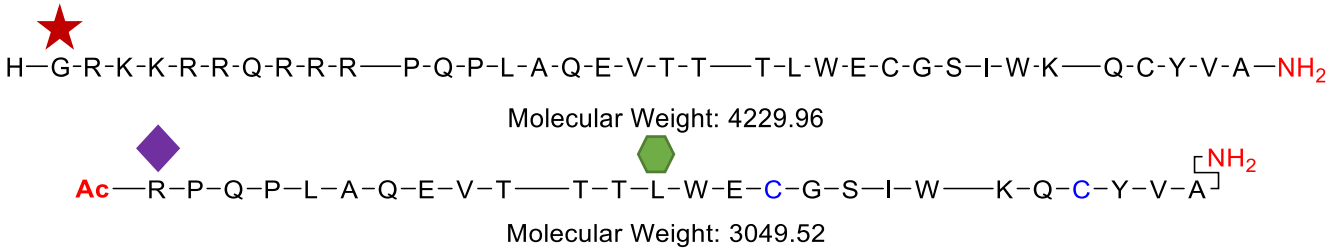


Figure S6. MALDI-TOF-MS results of crude peptide (TATDOCK *i,i+*7) using ChemMatrix® resin (0.5 mmol/g) under HBTU/DIPEA conditions and proposed mass identification.

^{19}F NMR: TFA-to-Ac salt exchange

To effectuate the transition from trifluoroacetate to acetate salt, the utilization of a potent anion resin, specifically AG1-X8 with quaternary ammonium functionality, was chosen. In pursuit of a thorough counter ion exchange, 245 mg of the resin was prepared within a 10 mL solid-phase peptide synthesis (SPPS) reactor for the trifluoroacetate to acetate salt conversion. This process involved successive triple rinses of the resin with 1.6M acetic acid (10 mL) and subsequent triple rinses with 0.16M acetic acid (10 mL). Following this, a peptide solution (20 mg in 4 mL of miliQ water) was carefully introduced onto the resin. After a 2-hour period of vigorous stirring, the resultant peptide-resin suspension underwent filtration, and the recovered liquid phase was isolated. The resin was subjected to dual washes with 1-2 mL of miliQ water. Subsequently, the combined solutions were subjected to pooling, and the isolated peptide (acetate salt) was obtained through freeze-drying. Afterward, the dried peptide was subjected to 19F-NMR analysis to confirm the conversion through salt exchange.

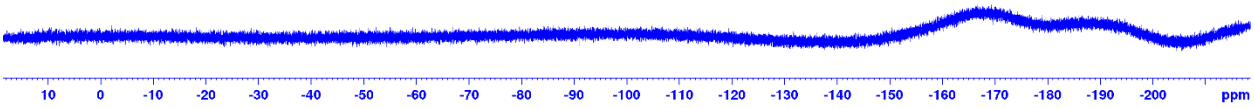
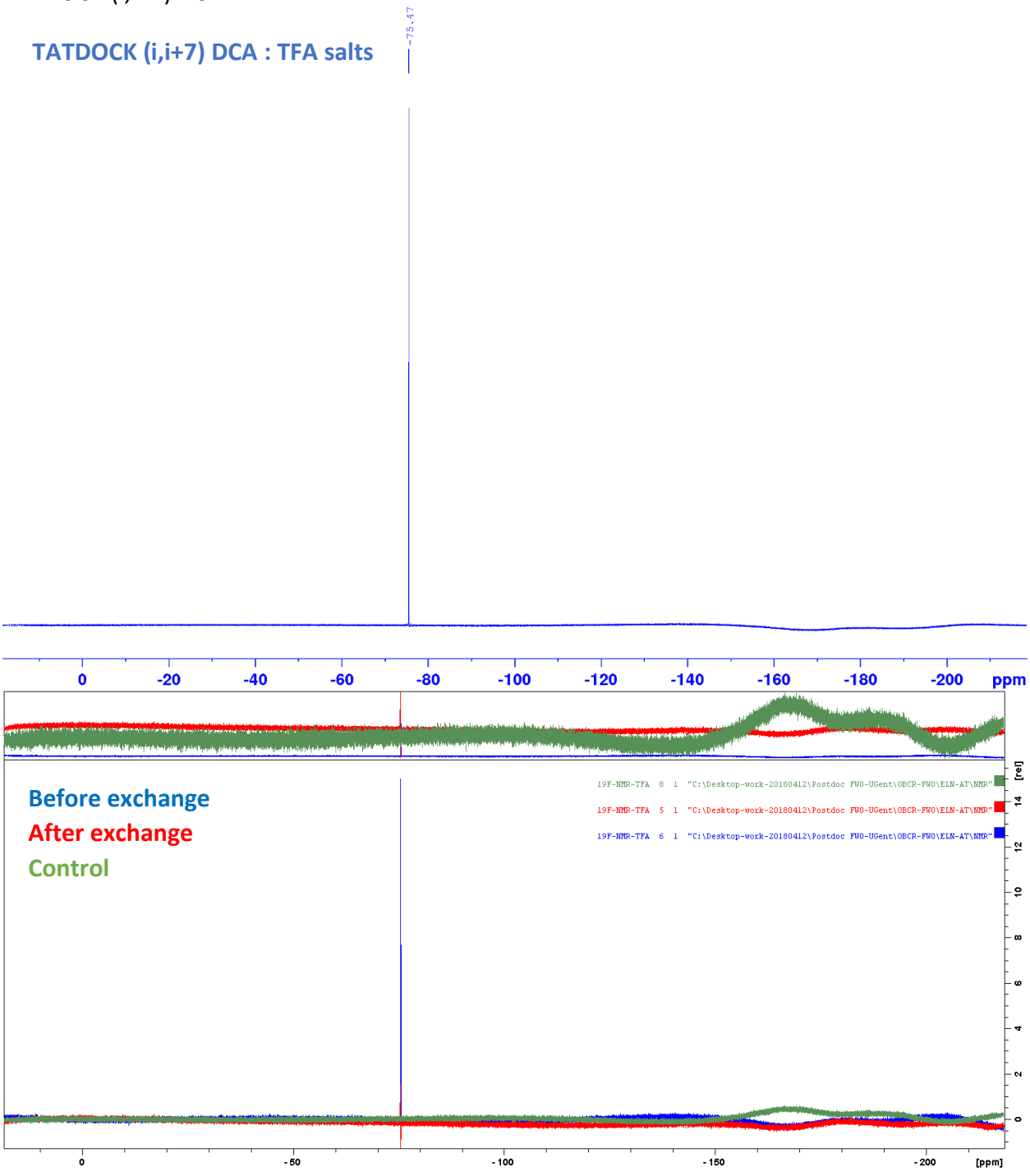


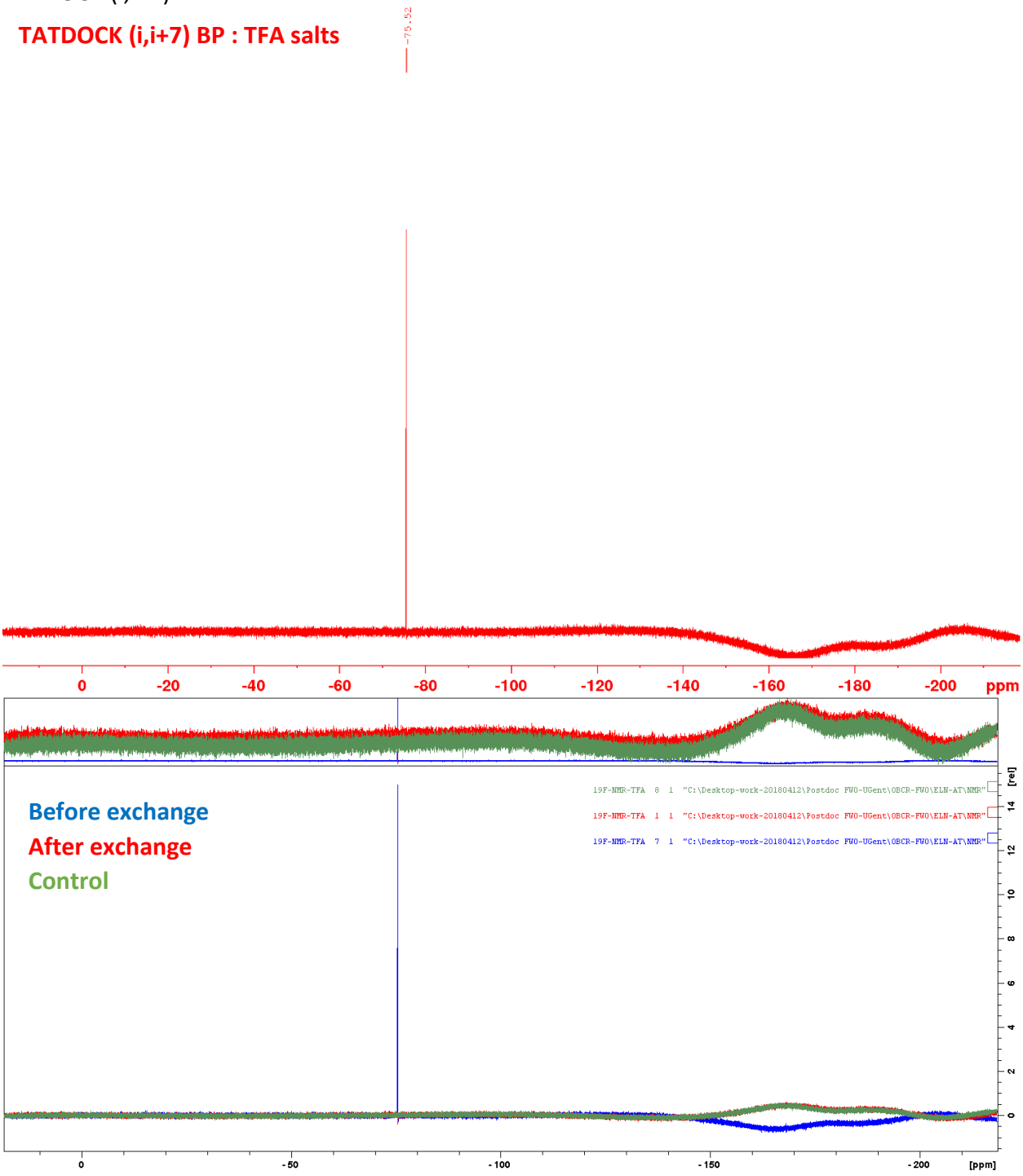
Figure S7. ^{19}F-NMR of deuterated oxide (D_2O) without any peptides (control experiment)

TATDOCK (i,i+7) DCA



TATDOCK (i,i+7) BP

TATDOCK (i,i+7) BP : TFA salts



IV. pH determination of TATDOCK peptides in milliQ water (pH 7.29)

Table S3. Overview pH of TATDOCK peptides

Compound	pH
TDWT	5.05
TD-i7	3.59
TD-i7 (Di S-S)	nd
TD-i7-DCA	3.59
TD-i7-BP	3.75
TD-i7-X	3.61
TD-i4	3.66
TD-i4-DCA	3.29
TD-i4-BP	3.63
TD-i4-X	3.66
TSWT	4.02
TS-i7	3.76
TS-i7-DCA	2.30
TS-i7-BP	2.24
TS-i7-X	2.26

nd = not determined

The observed pH was measured at 3mg/mL concentration for each peptide in MQ water pH 7.29

V. Observed solubility value in MQ (pH = 7.29)

TD-i7 -> at least 4.6 mg/ml (4.6 mg in 1.0 mL of MQ)
TD-i7-BP -> at least 3.7 mg/ml (1.89 mg in 0.5 mL of MQ)
TD-i7-DCA -> at least 3.4 mg/ml (0.69 mg in 0.2 mL of MQ)
TD-i7-X -> at least 8.7 mg/ml (0.87mg in 0.1 mL of MQ)
TS-i7 -> at least 8.4 mg/ml (25.1 mg in 3.0 mL of MQ)
TS-i7-BP -> at least 2.3 mg/ml (4.53 mg in 2.0 mL of MQ)
TS-i7-DCA -> at least 5.2 mg/ml (2.6 mg in 0.5 mL of MQ)
TS-i7-X -> at least 10.0 mg/ml (3.5 mg in 0.35 mL of MQ)
TS-WT -> at least 6.4 mg/ml (5.1 mg in 0.8 mL of MQ)
TD-WT -> at least 7.4 mg/ml (3.74 mg in 0.5 mL of MQ)
TD-i4 -> at least 16.9 mg/ml (3.28 mg in 0.25 mL of MQ)
TD-i4-BP -> at least 7.9 mg/ml (1.58 mg in 0.20 mL of MQ)

TD-i4-DCA -> at least 13.6 mg/ml (1.36 mg in 0.10 mL of MQ)
TD-i4-X -> at least 15.6 mg/ml (3.89 mg in 0.25 mL of MQ)
DOCK-i7 -> lower than 40 μg/ml (0.16 mg in 4.0 mL of MQ)* **poor solubility in water**
DOCK-i7-DCA and DOCK-i7 BP: ND
DOCK-i4 -> lower than 38 μg/ml (1.0 mg in 26 mL of MQ)* **poor solubility in water**
* not completely dissolved in MQ, ND = not determined

Notes:

1) Most peptides were obtained after semi-prep. HPLC
2) DOCK (i,i+7 and i,i+4) peptides dissolved well in 2:1 MeCN and water
3) In general, TD/TS stapled peptides have good water solubility in the range of **3.4-16.9 mg/ml**

VI. Circular Dichroism (CD) Spectroscopy results

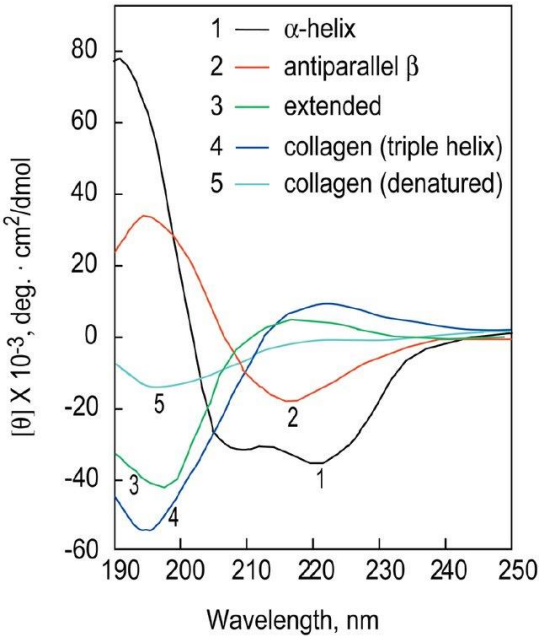


Figure S8. Characteristic pattern for circular dichroism (CD) spectra of polypeptides and proteins with some representative secondary structures, this figure was taken from *Nature Protocols,* 2006.[51]

Table S4. Ratios of Ellipticities at 222 and 208 nm

Compound	$[\theta]_{222}/[\theta]_{208}$ in MQ	$[\theta]_{222}/[\theta]_{208}$ in 50% TFE
TDWT	0.45	0.60
TD-i7	0.52	0.70
TD-i7-DCA	0.50	0.70
TD-i7-BP	1.06	0.68
TD-i7-X	0.39	0.65
TD-i4	0.47	0.63
TD-i4-DCA	1.13	0.73
TD-i4-BP	0.84	0.43
TD-i4-X	0.29	0.70
TSWT	0.43	0.39
TS-i7	0.47	0.41
TS-i7-DCA	0.58	0.48
TS-i7-BP	0.88	0.43
TS-i7-X	0.45	0.42

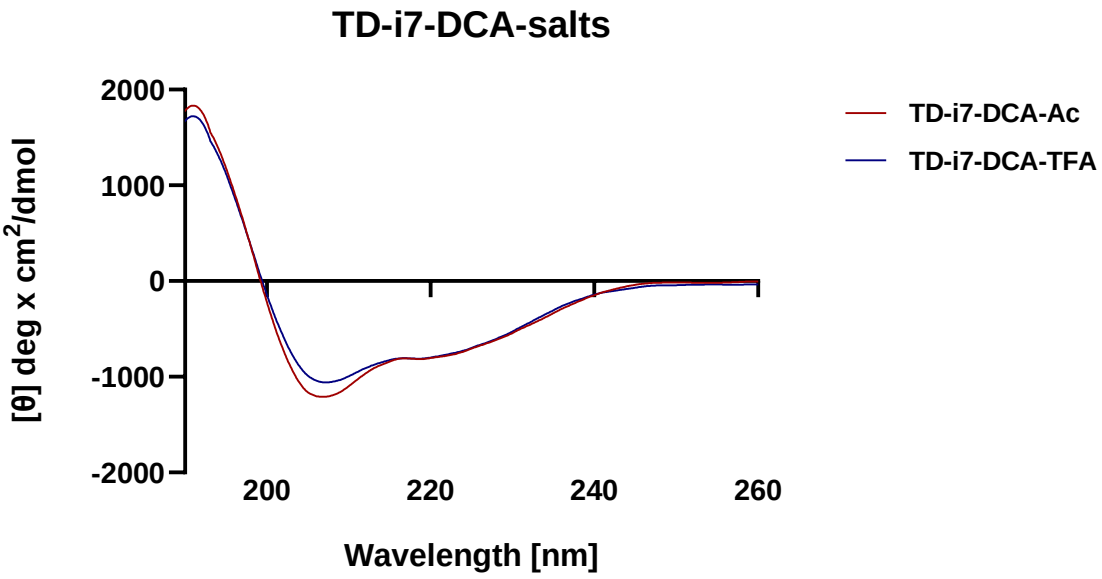


Figure S9. CD spectra of TATDOCK-i7-DCA (salt exchanged Acetate vs TFA). The peptides were dissolved in 1:1 TFE/H_2O at a final concentration of 20 µM.

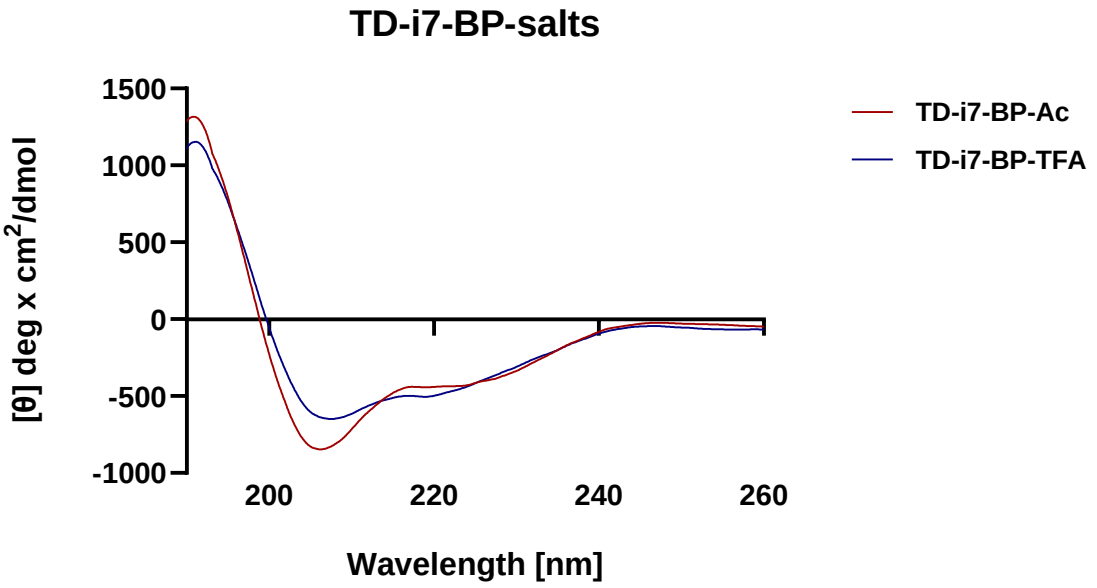


Figure S10. CD spectra of TATDOCK-i7-BP (salt exchanged Acetate vs TFA). The peptides were dissolved in 1:1 TFE/H_2O at a final concentration of 20 µM.

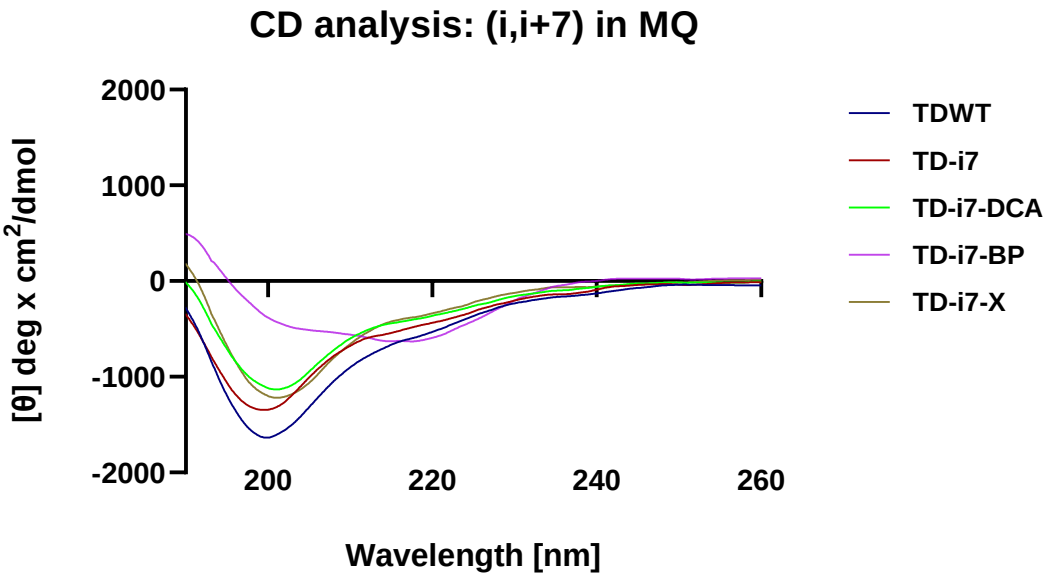


Figure S11. CD spectra of TATDOCK (wt) and TATDOCK (i,i+7) series in miliQ water (pH 7.29) at a final concentration of 20 µM.

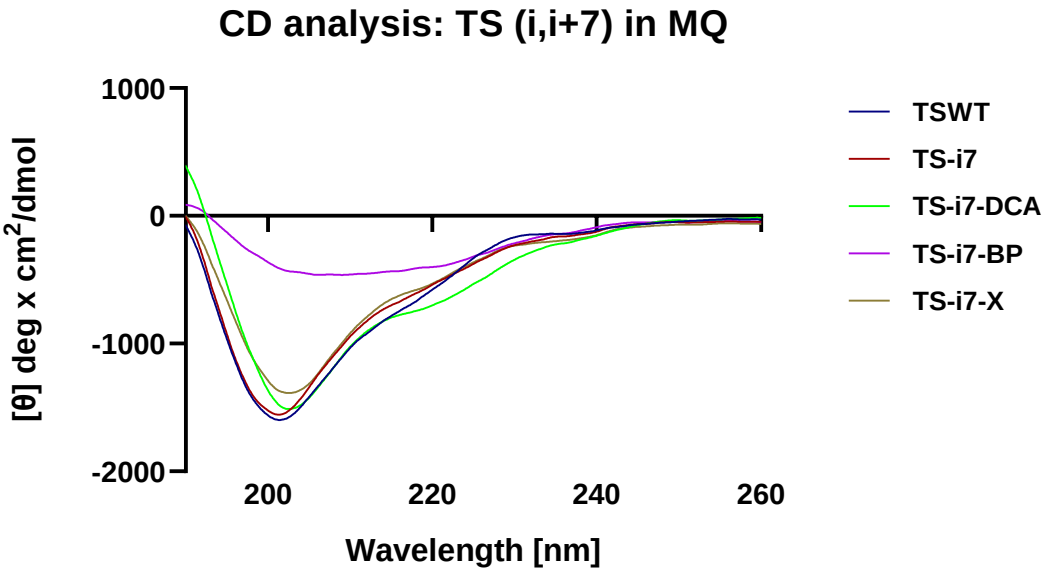


Figure S12. CD spectra of TATDOCK scrambled (wt) and TATDOCK scrambled (i,i+7) series in miliQ water (pH 7.29) at a final concentration of 20 µM.

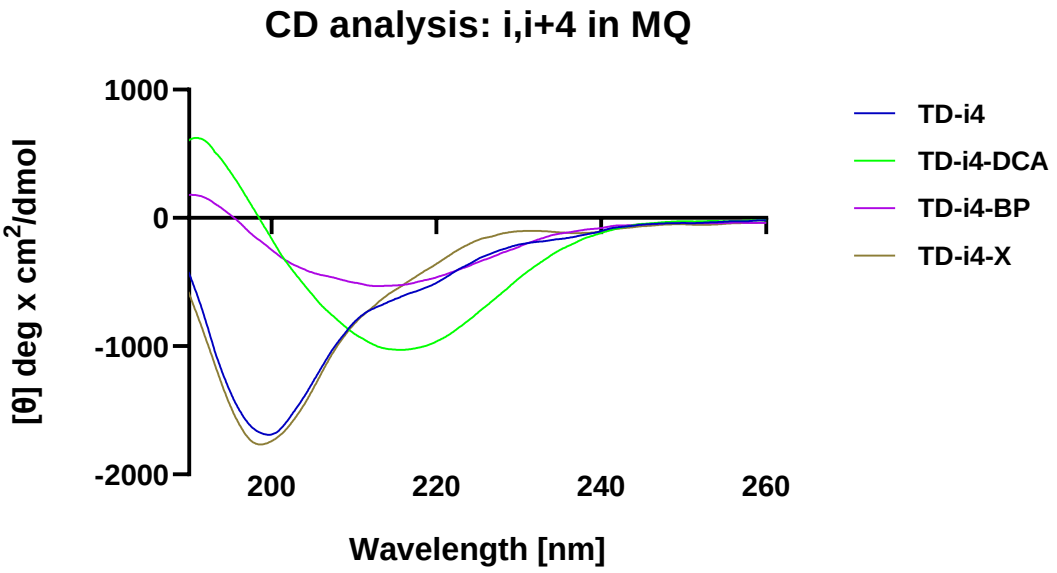


Figure S13. CD spectra of TATDOCK (i,i+4) series in miliQ water (pH 7.29) at a final concentration of 20 µM.

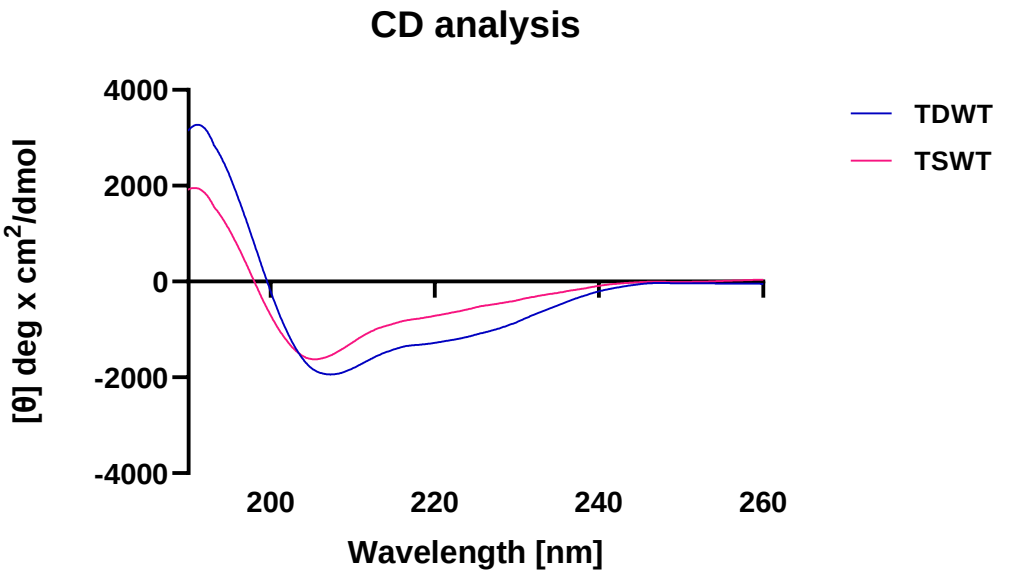


Figure S14. Comparison of CD spectra of TATDOCK (wt) and TATDOCK scrambled (wt). The peptides were dissolved in 1:1 TFE/H_2O at a final concentration of 20 µM.

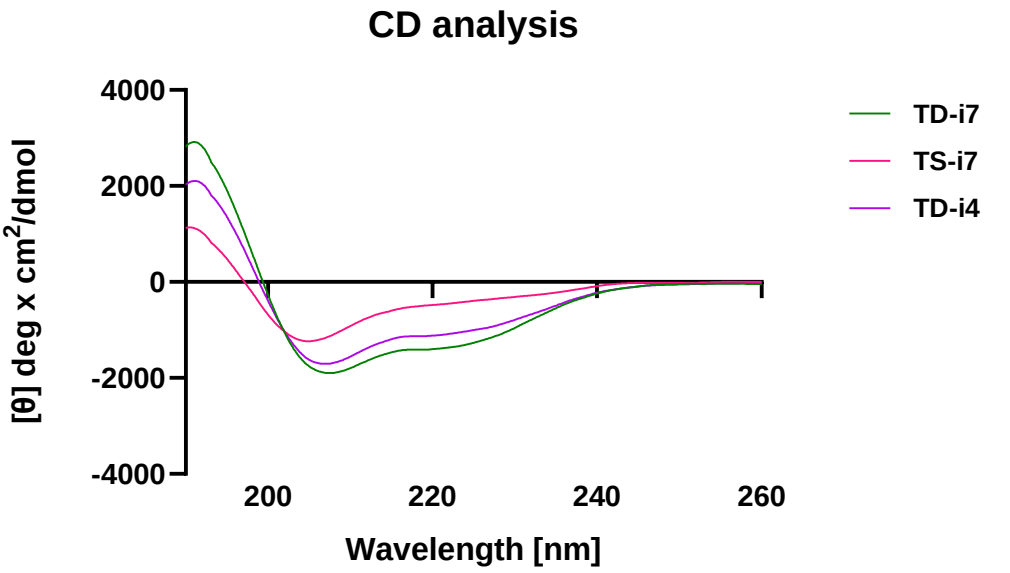


Figure S15. Comparison of CD spectra of TATDOCK (i,i+7), TATDOCK scrambled (i,i+7) and TATDOCK (i,i+4). The peptides were dissolved in 1:1 TFE/H_2O at a final concentration of 20 µM.

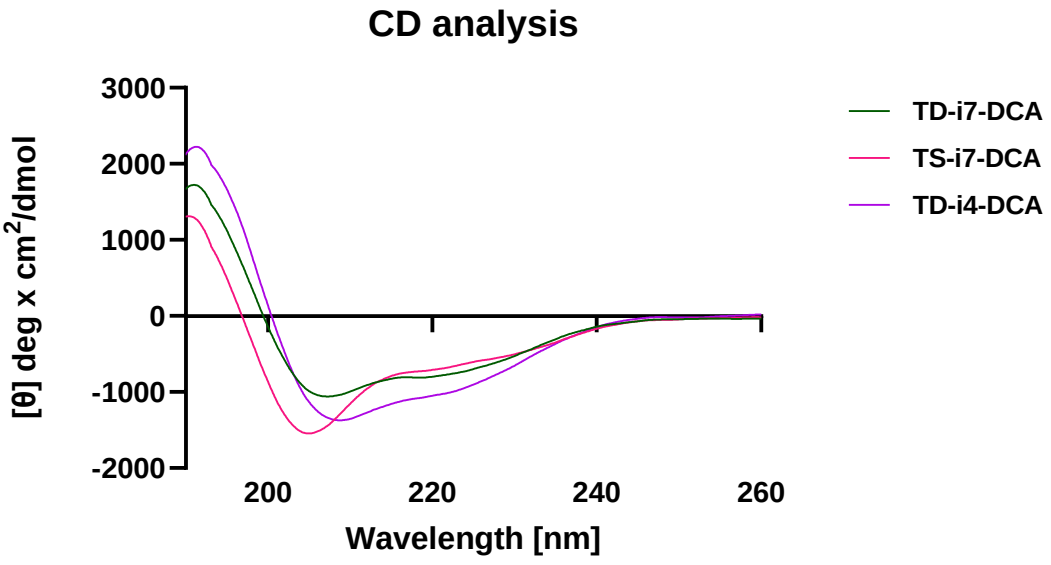


Figure S16. Comparison of CD spectra of TATDOCK (I,i+7), TATDOCK scrambled (i,i+7) and TATDOCK (i,i+4) conjugated with DCA moiety. The peptides were dissolved in 1:1 TFE/H_2O at a final concentration of 20 µM.

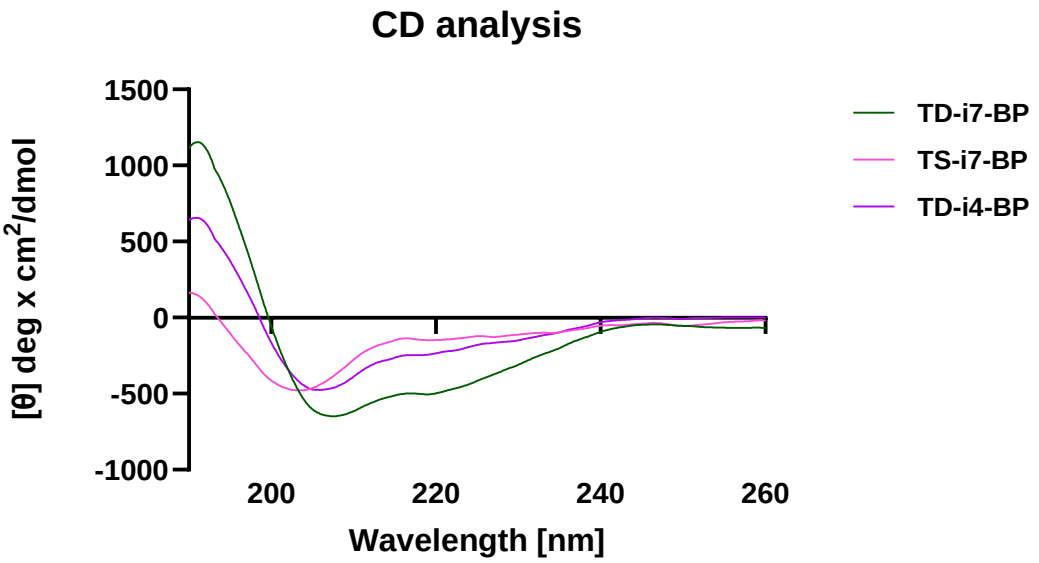


Figure S17. Comparison of CD spectra of TATDOCK (I,i+7), TATDOCK scrambled (i,i+7) and TATDOCK (i,i+4) conjugated with BP moiety. The peptides were dissolved in 1:1 TFE/H_2O at a final concentration of 20 µM.

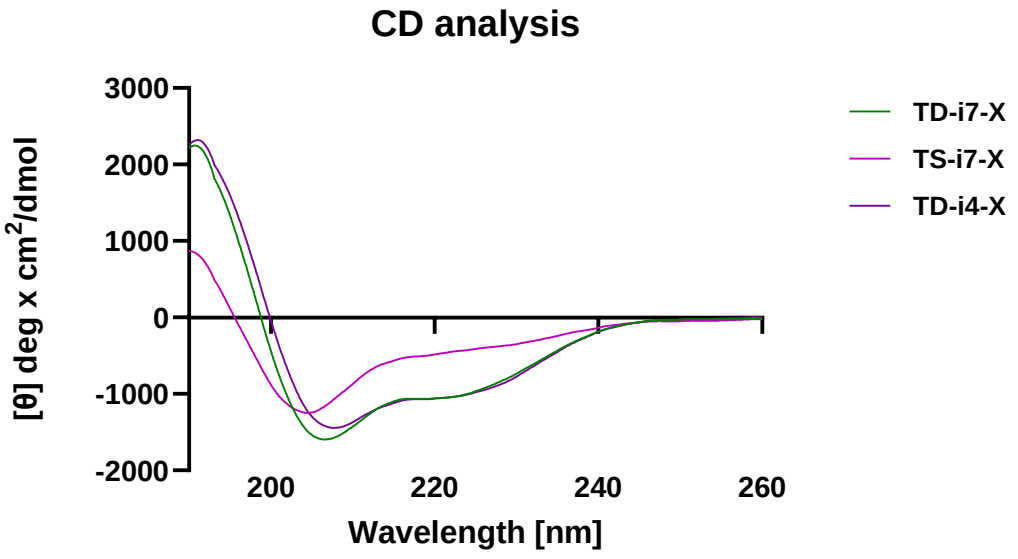


Figure S18. Comparison of CD spectra of TATDOCK (I,i+7), TATDOCK scrambled (i,i+7) and TATDOCK (i,i+4) conjugated with X moiety. The peptides were dissolved in 1:1 TFE/H_2O at a final concentration of 20 µM.