

Supporting Information

Structure Activity Relationship Studies to Probe the Phosphoprotein Binding Site on the Carboxy Terminal Domains of the Breast Cancer Susceptibility Gene 1

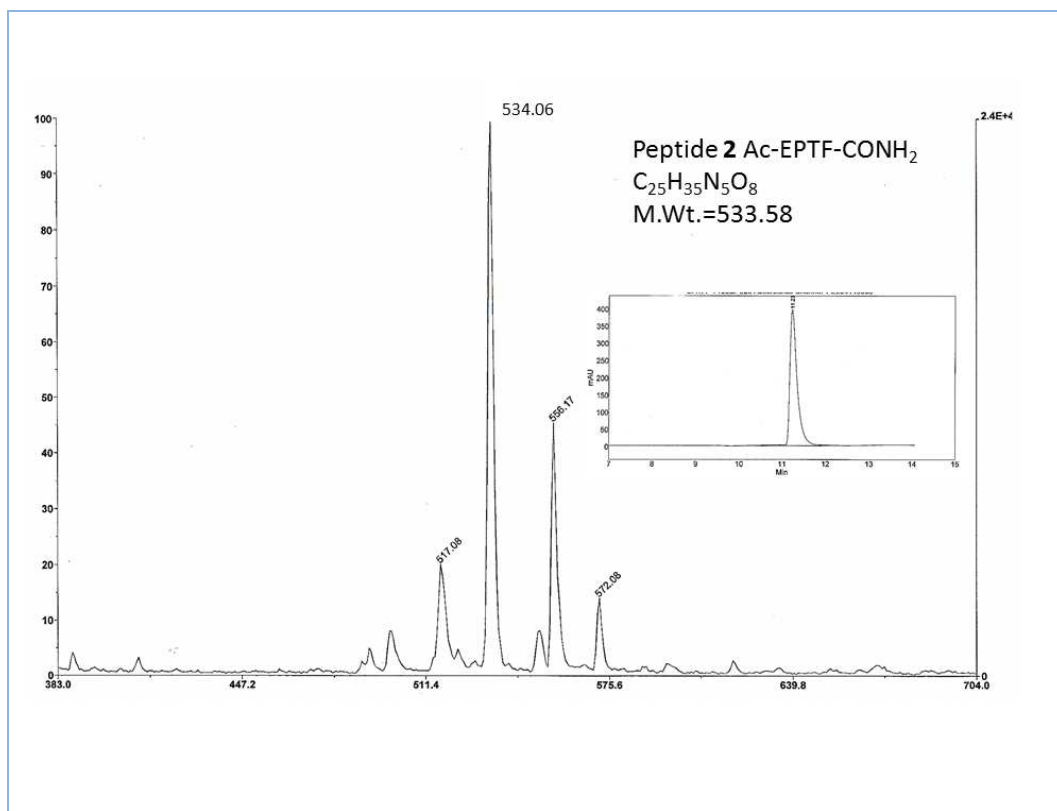
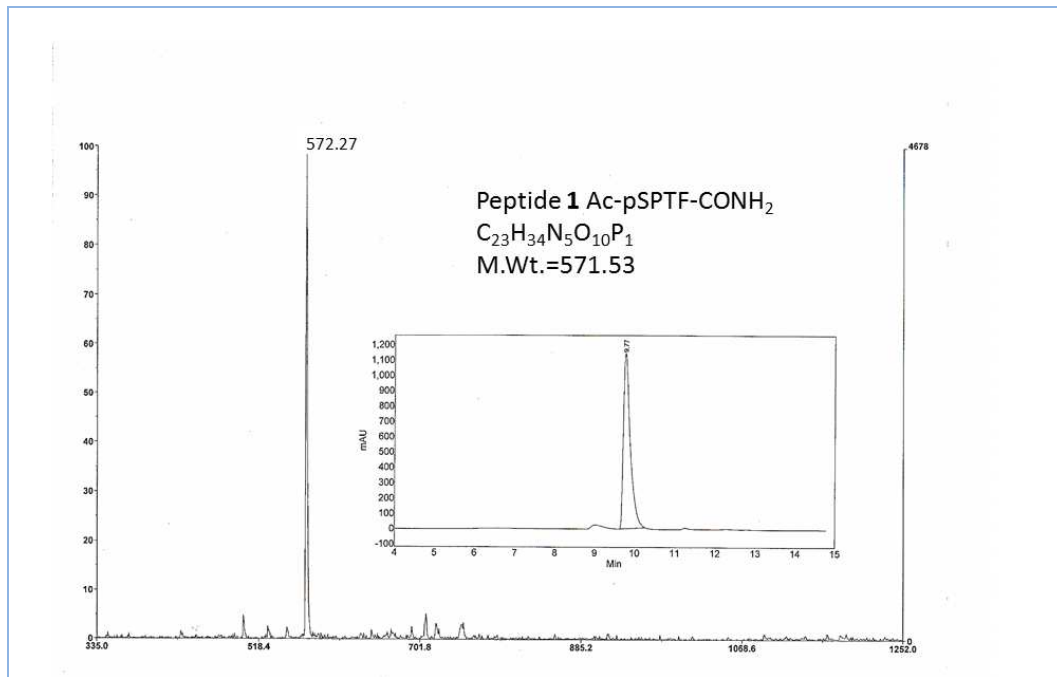
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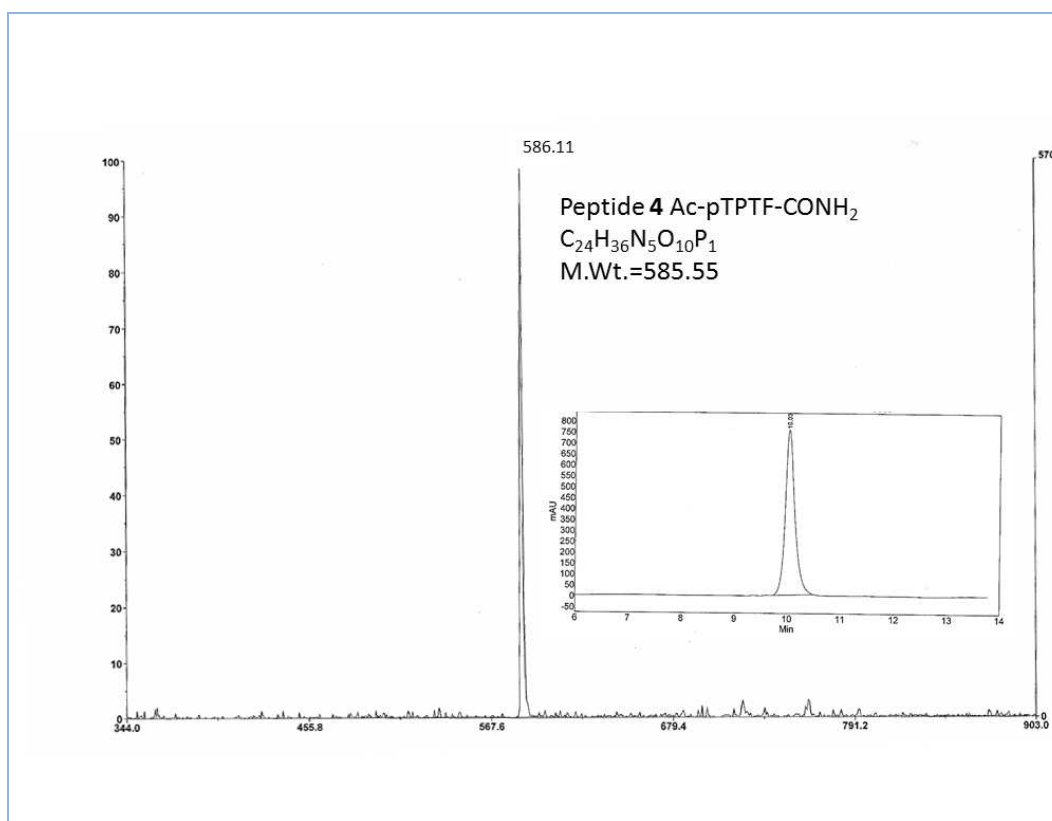
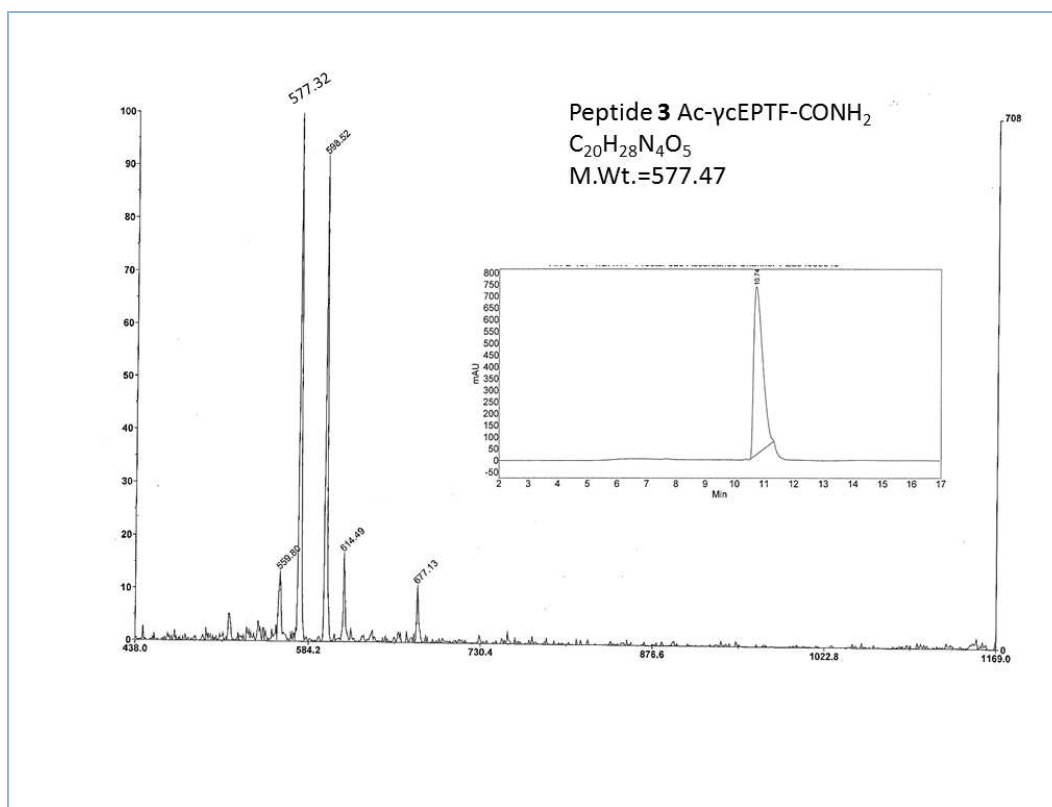
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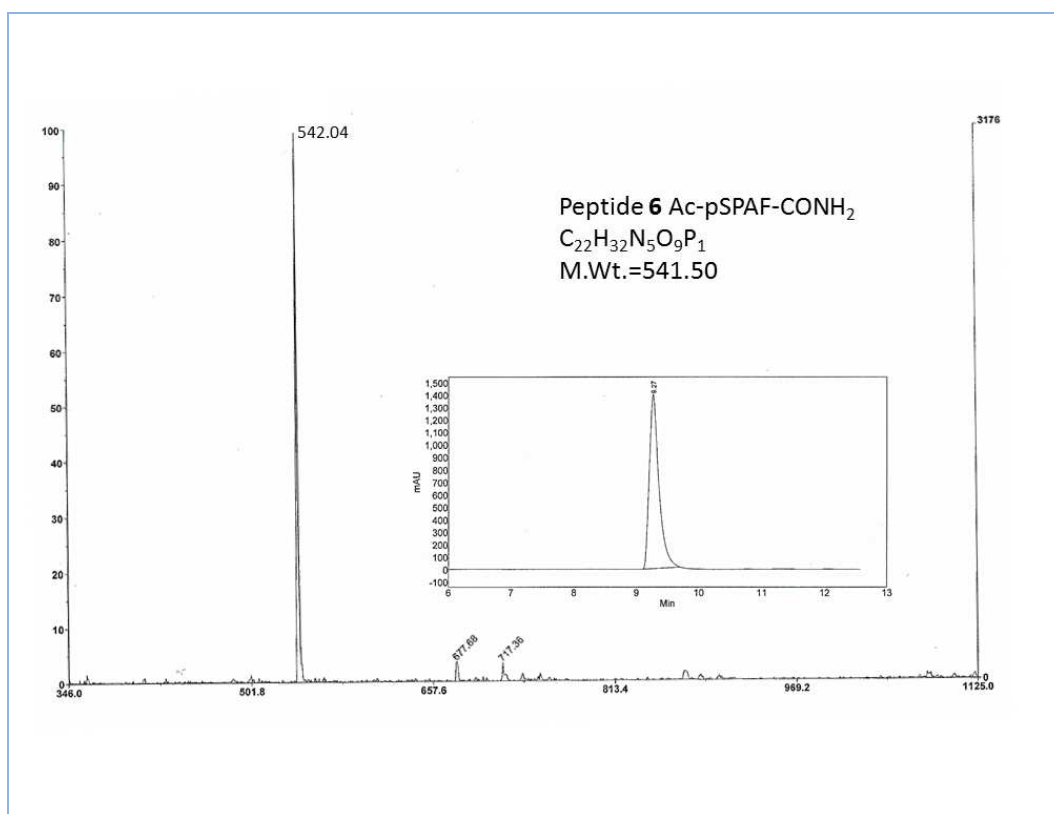
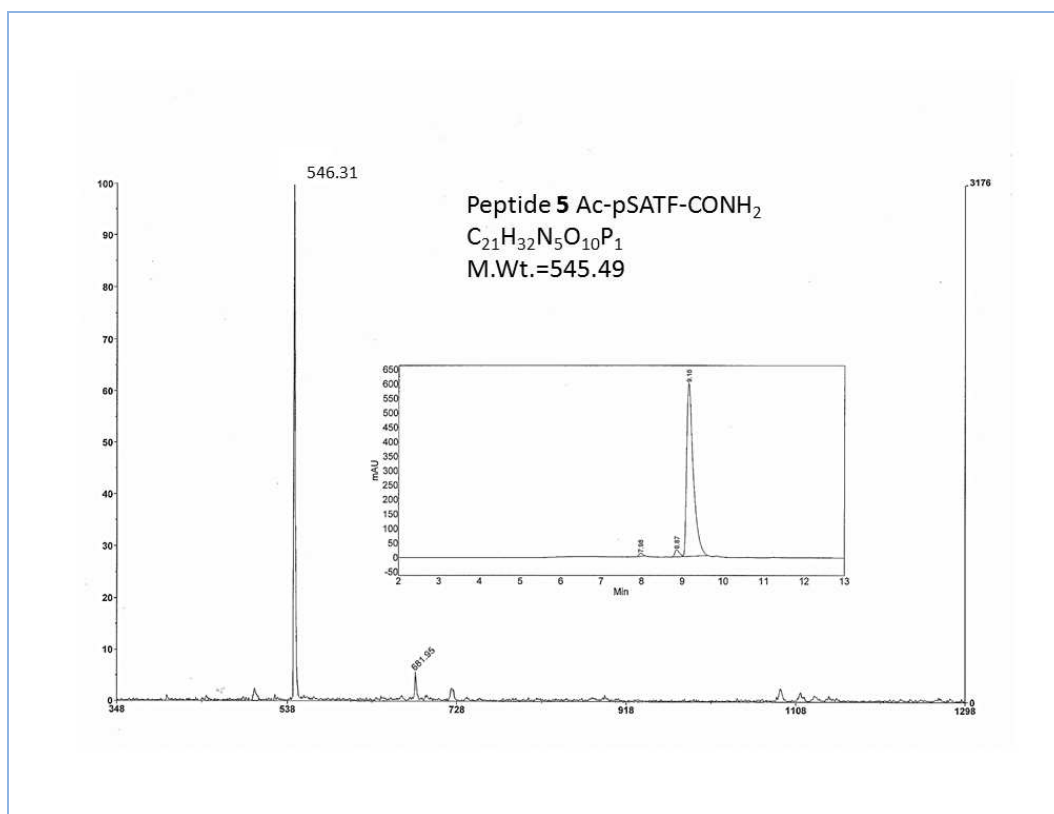
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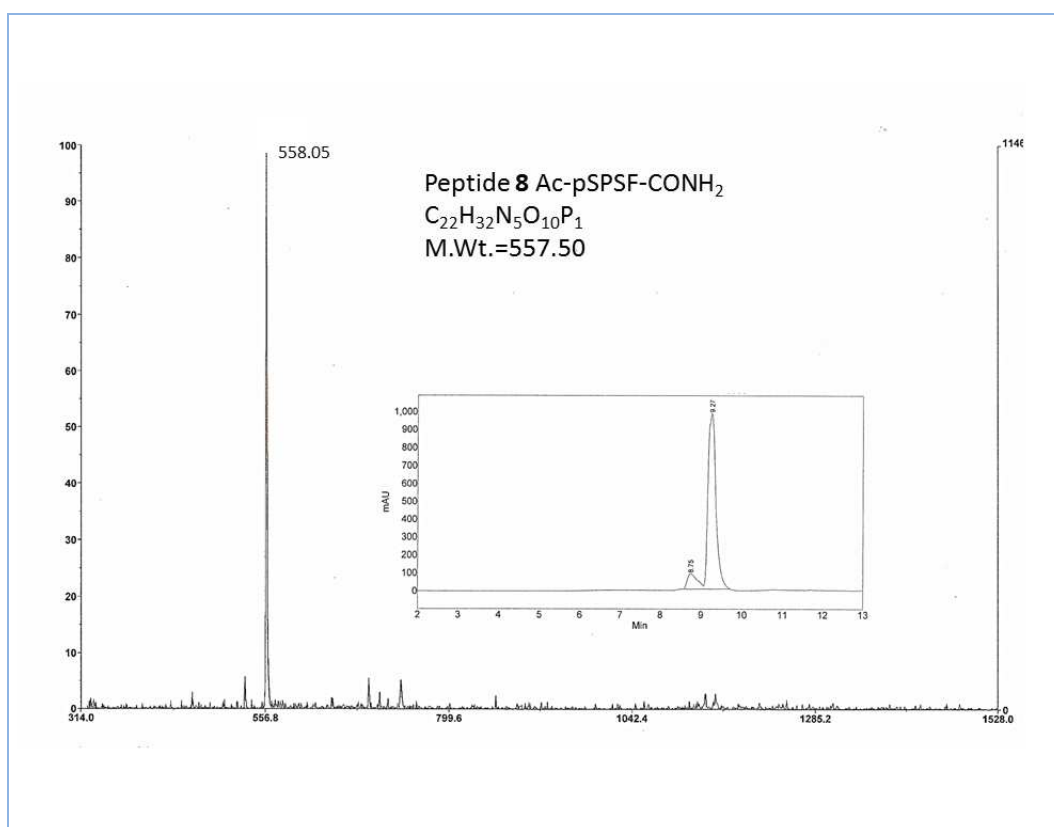
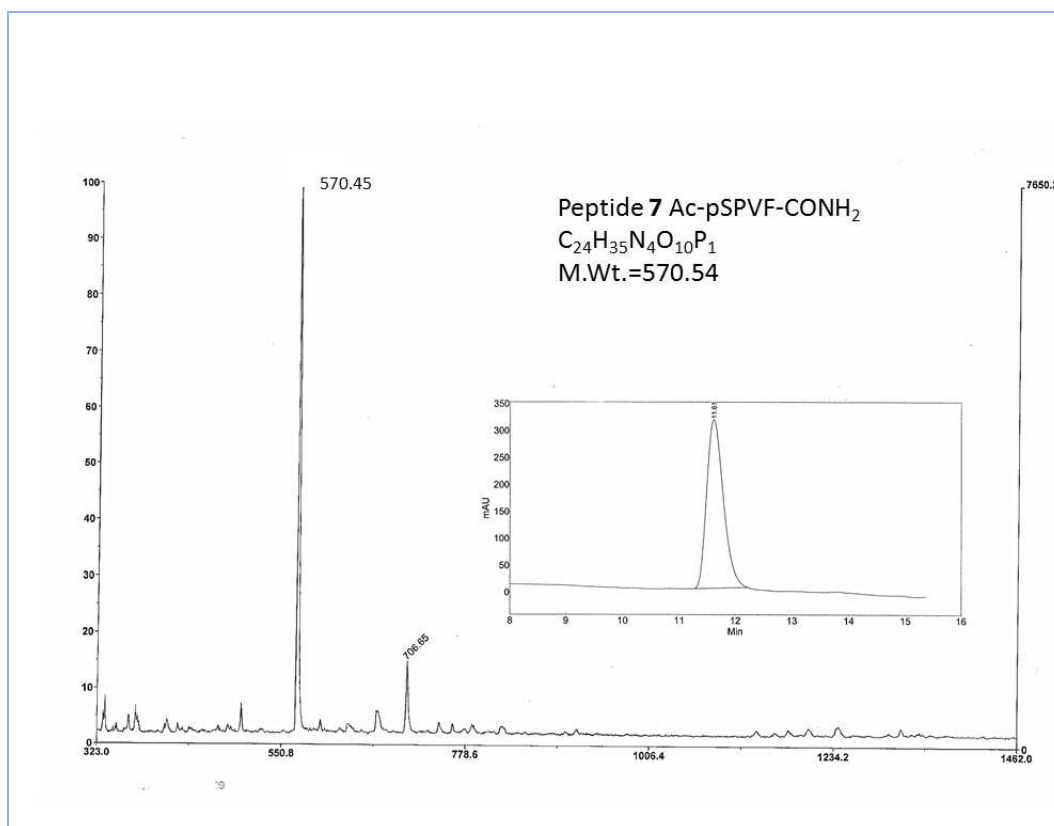
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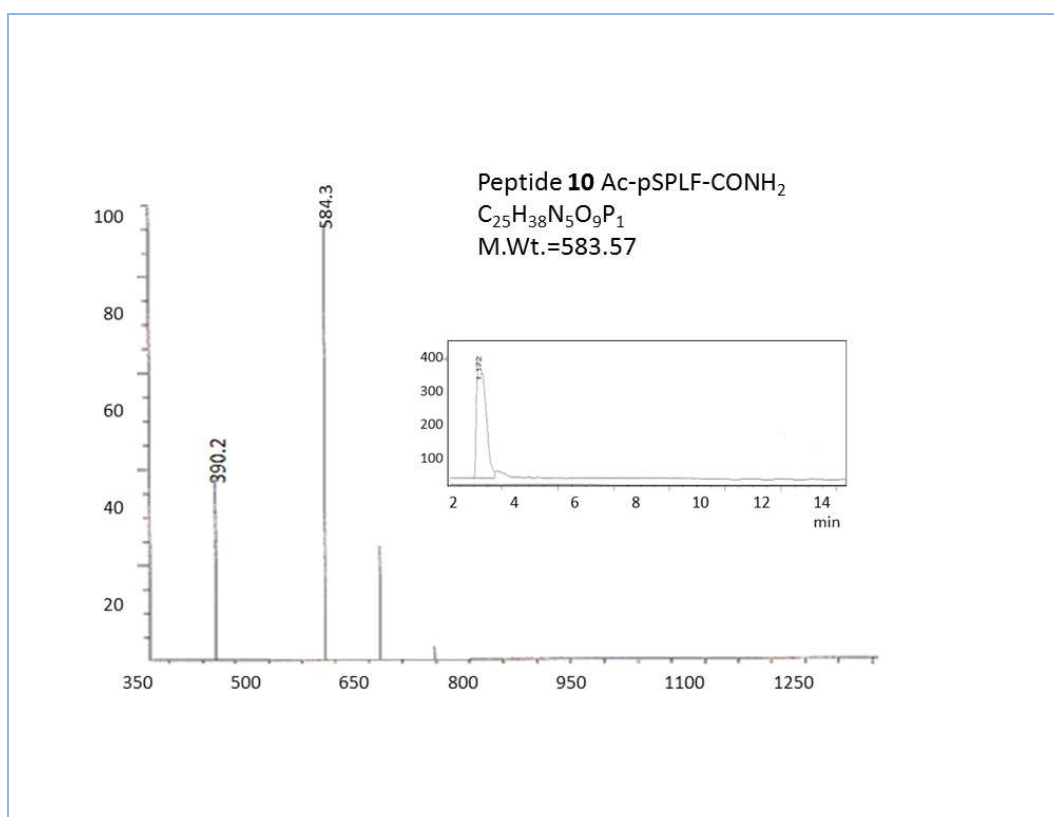
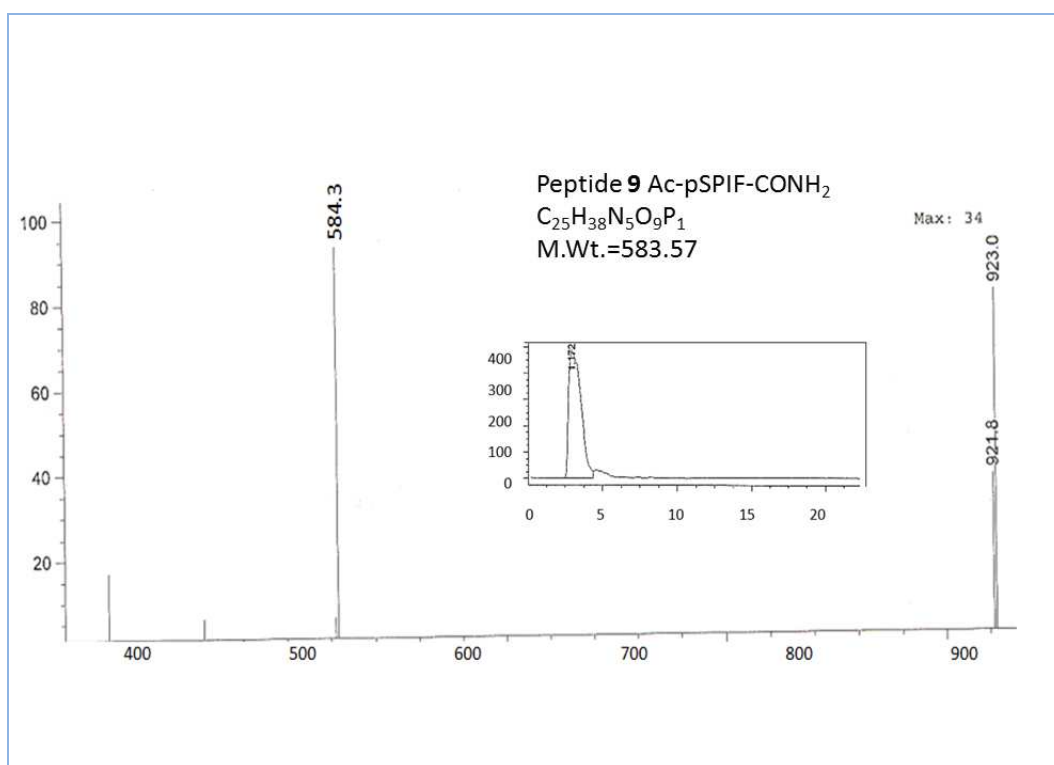
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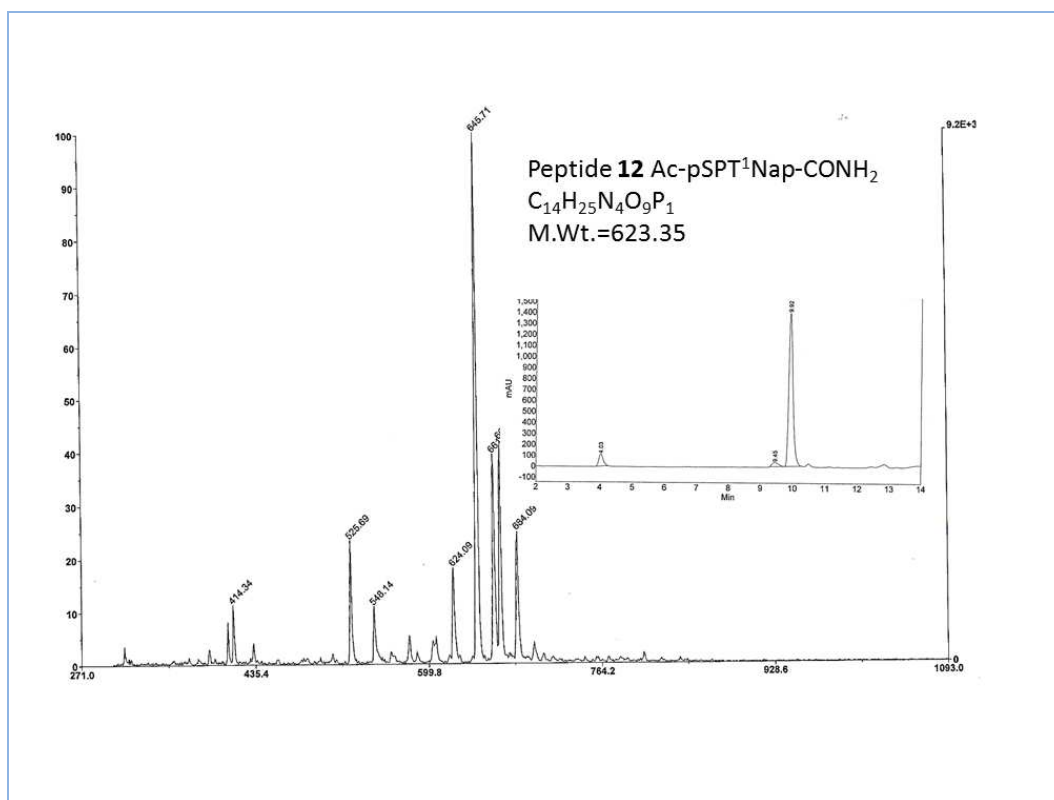
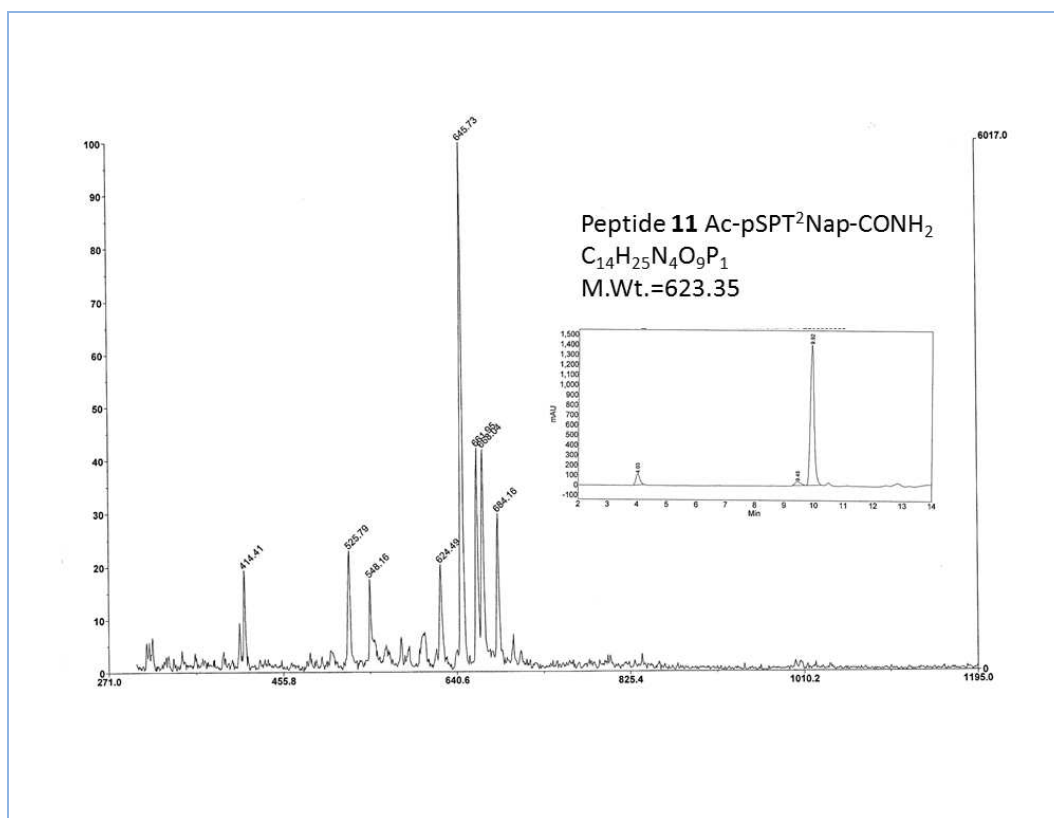


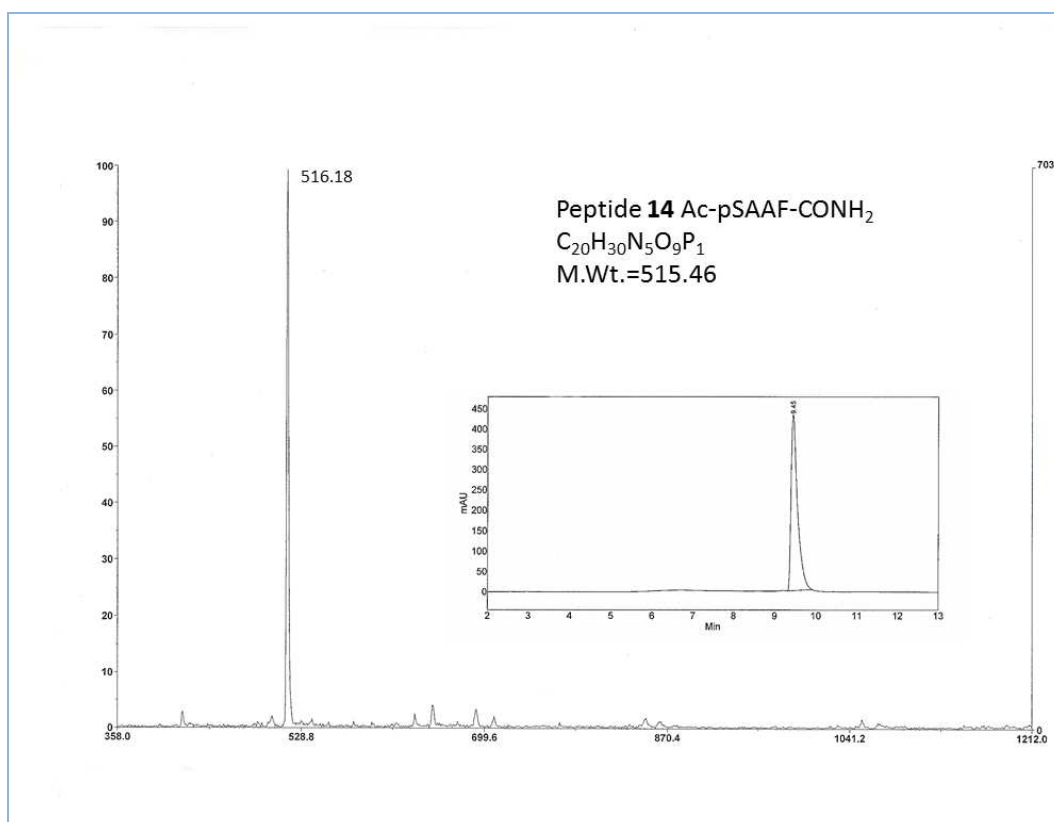
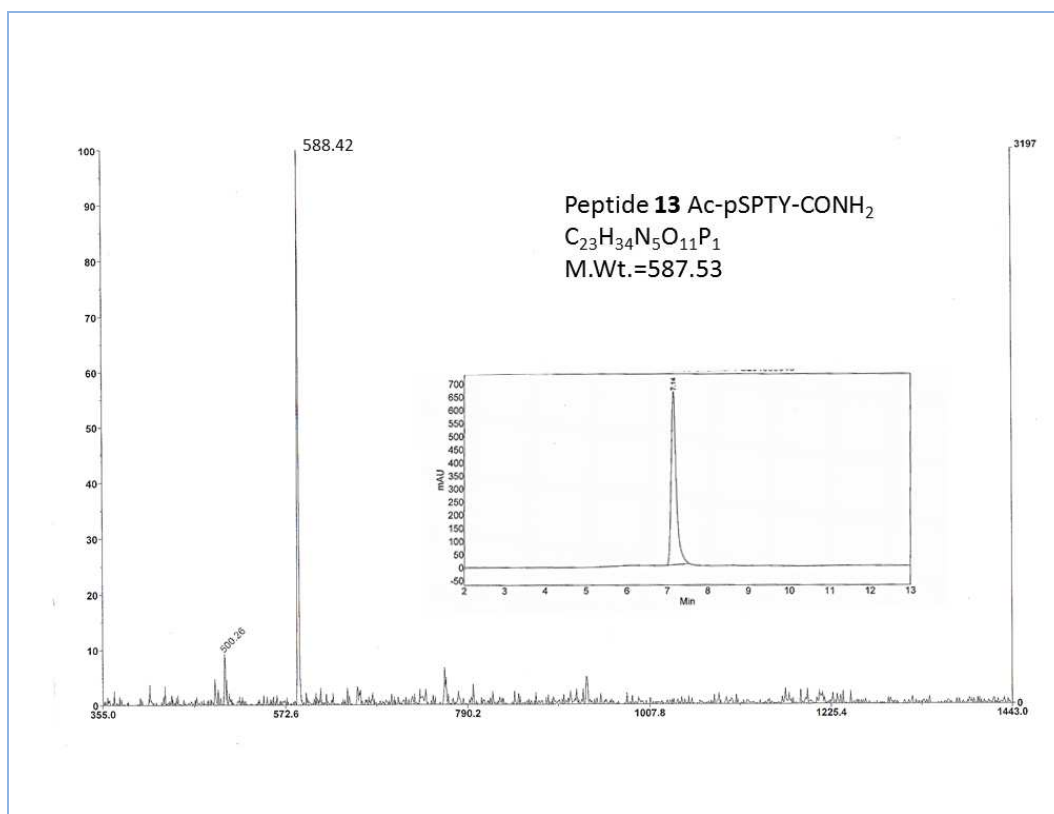


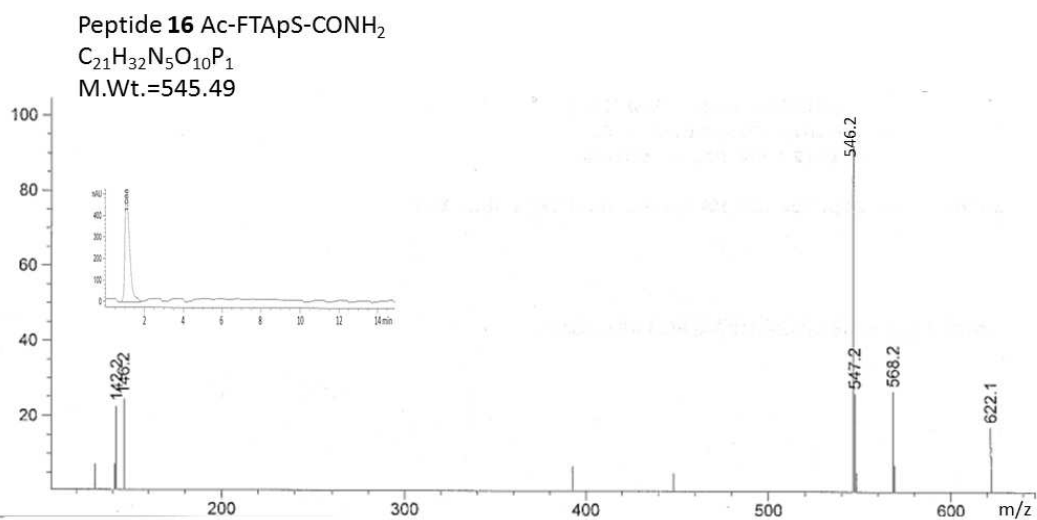
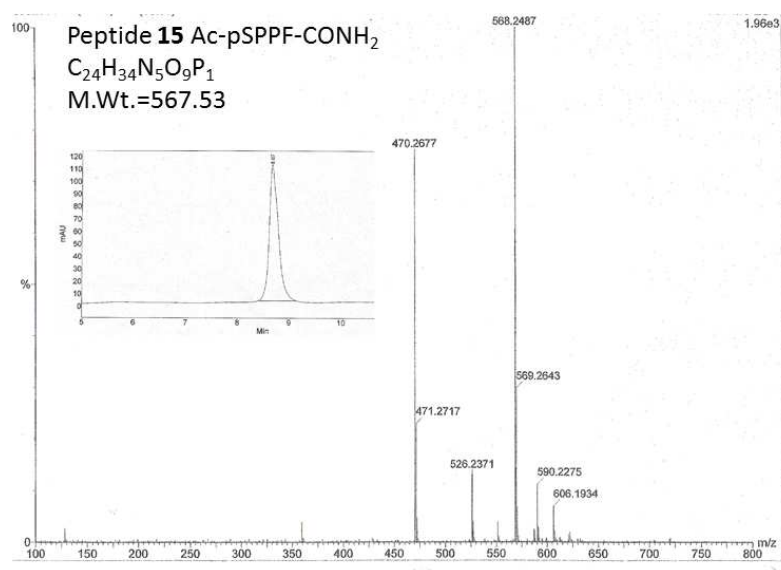


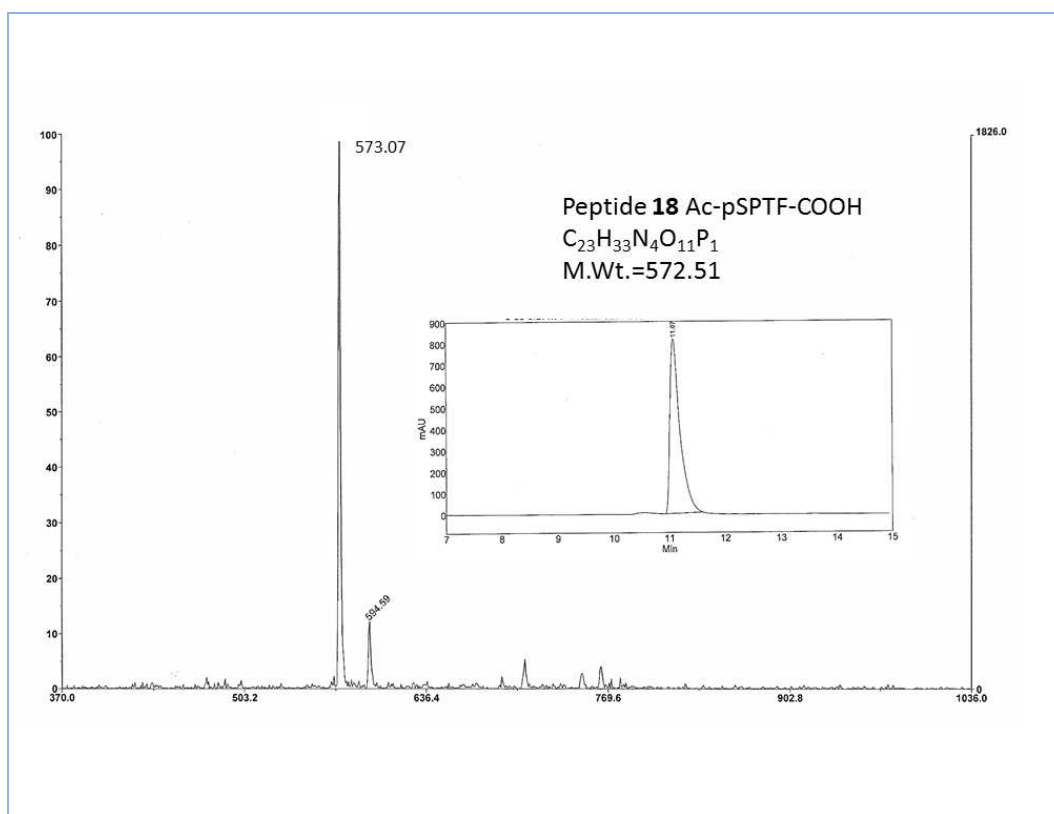
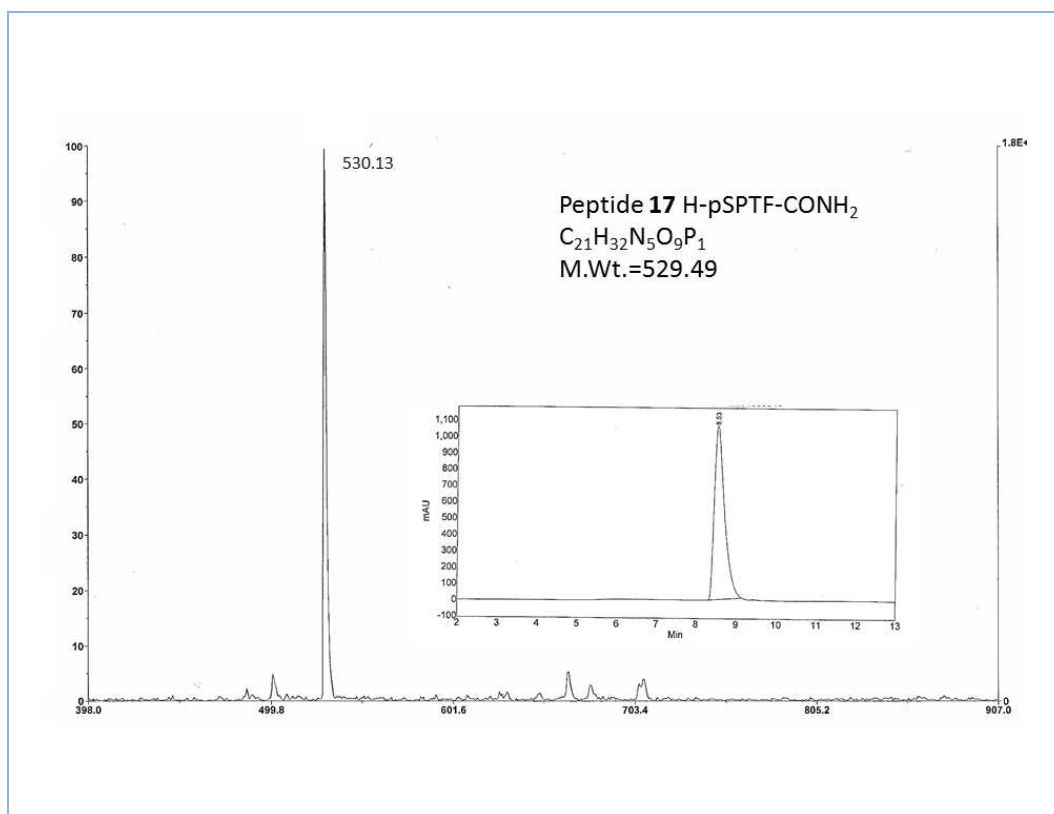












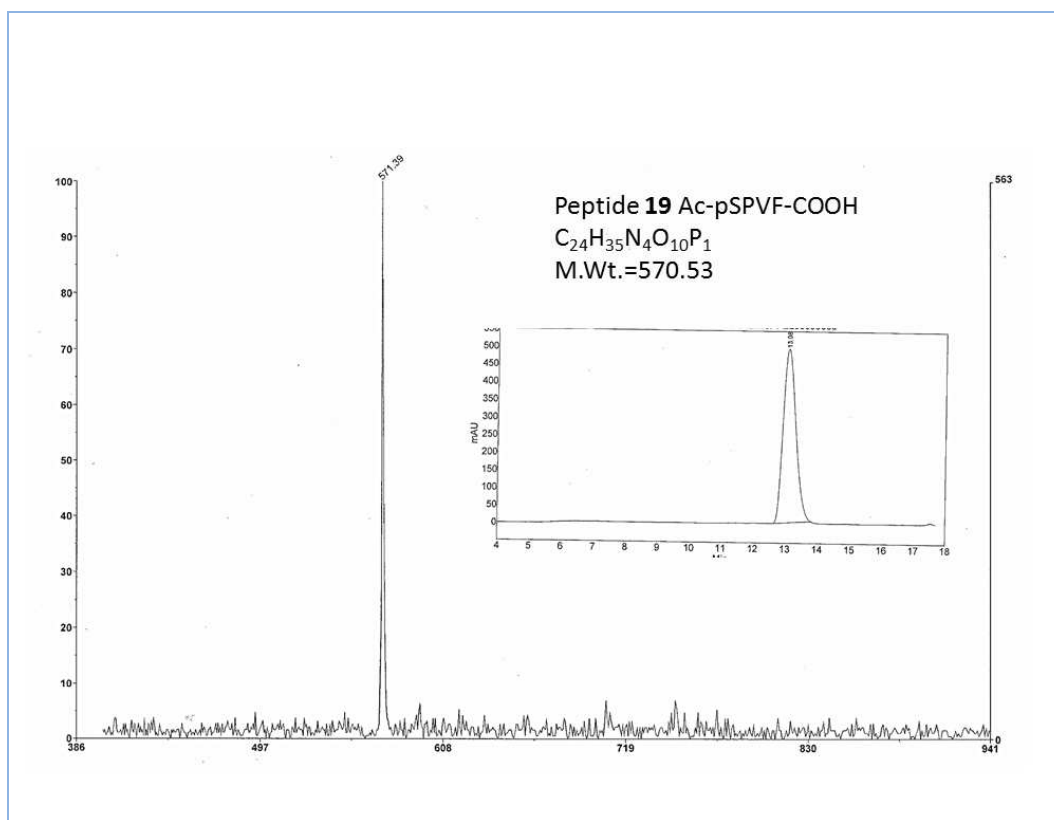


Table S1. Thermodynamic parameters of pSPXF-BRCT(BRCA1) interactions derived from ITC studies

Peptide	Temperature (K)	N	$K_a \times 10^5$ (M ⁻¹)	$-\Delta G^a$ (kcal/mol)	$-\Delta H$ (kcal/mol)	$-T\Delta S^a$ (kcal/mol)
1	298	0.97 ± 0.01	3.99 ± 0.12	7.61 ± 0.03	13.76 ± 0.13	6.13 ± 0.03
1	301	0.82 ± 0.01	2.98 ± 0.09	7.51 ± 0.03	14.90 ± 0.20	7.37 ± 0.03
1	304	0.85 ± 0.01	2.47 ± 0.11	7.47 ± 0.04	15.56 ± 0.31	8.07 ± 0.02
1	307	0.76 ± 0.03	1.82 ± 0.15	7.36 ± 0.07	17.58 ± 0.85	10.21 ± 0.02
1	310	0.78 ± 0.04	1.44 ± 0.15	7.29 ± 0.09	17.81 ± 1.29	10.50 ± 0.03
18	298	0.83 ± 0.01	51.8 ± 4.58	9.12 ± 0.07	14.56 ± 0.12	5.42 ± 0.04
18	301	0.80 ± 0.01	38.0 ± 3.50	9.03 ± 0.08	15.28 ± 0.15	6.23 ± 0.04
18	303	0.79 ± 0.01	36.6 ± 1.83	9.07 ± 0.04	15.67 ± 0.09	6.57 ± 0.04
18	308	0.71 ± 0.02	21.4 ± 6.05	8.86 ± 0.25	16.97 ± 0.69	8.07 ± 0.05
18	310	0.70 ± 0.01	17.8 ± 1.30	8.83 ± 0.06	18.61 ± 0.21	9.76 ± 0.03
7	298	0.91 ± 0.01	6.18 ± 0.21	7.87 ± 0.03	18.34 ± 0.19	10.45 ± 0.03
19	298	0.91 ± 0.01	34.7 ± 1.17	8.89 ± 0.02	11.05 ± 0.04	2.14 ± 0.03

^a ΔG and ΔS were calculated by the following equations, respectively: $\Delta G = -RT \ln K_a$; $T\Delta S = \Delta H - \Delta G$

Figures

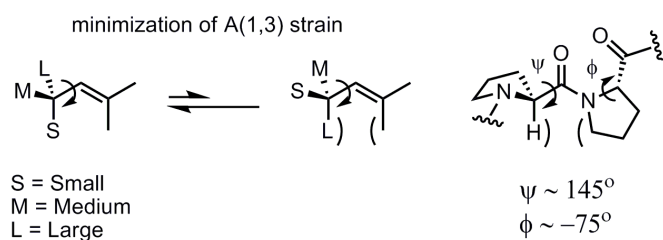


Figure S1. Minimization of pseudo A(1,3) strain in Pro-Pro

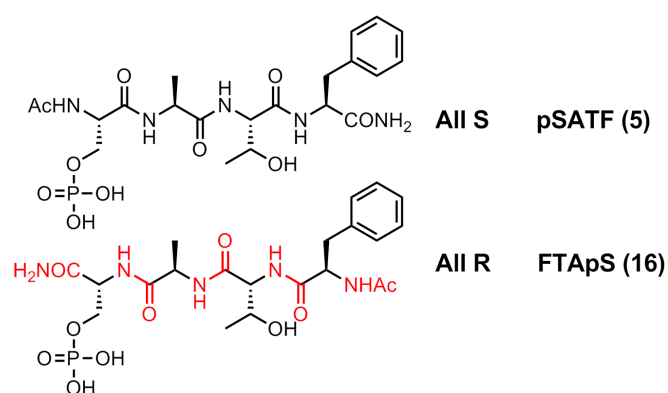


Figure S2. Reversing the amide bonds to probe for backbone effects on BRCT(BRCA1) binding.

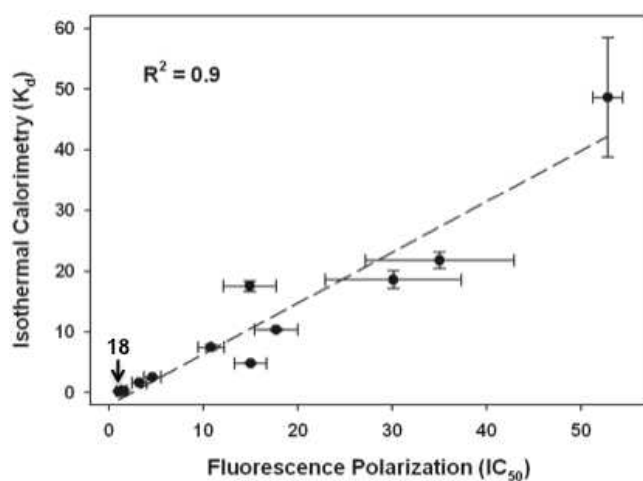


Figure S3. Correlation between the IC_{50} values (FP assay) and K_d values (ITC studies).

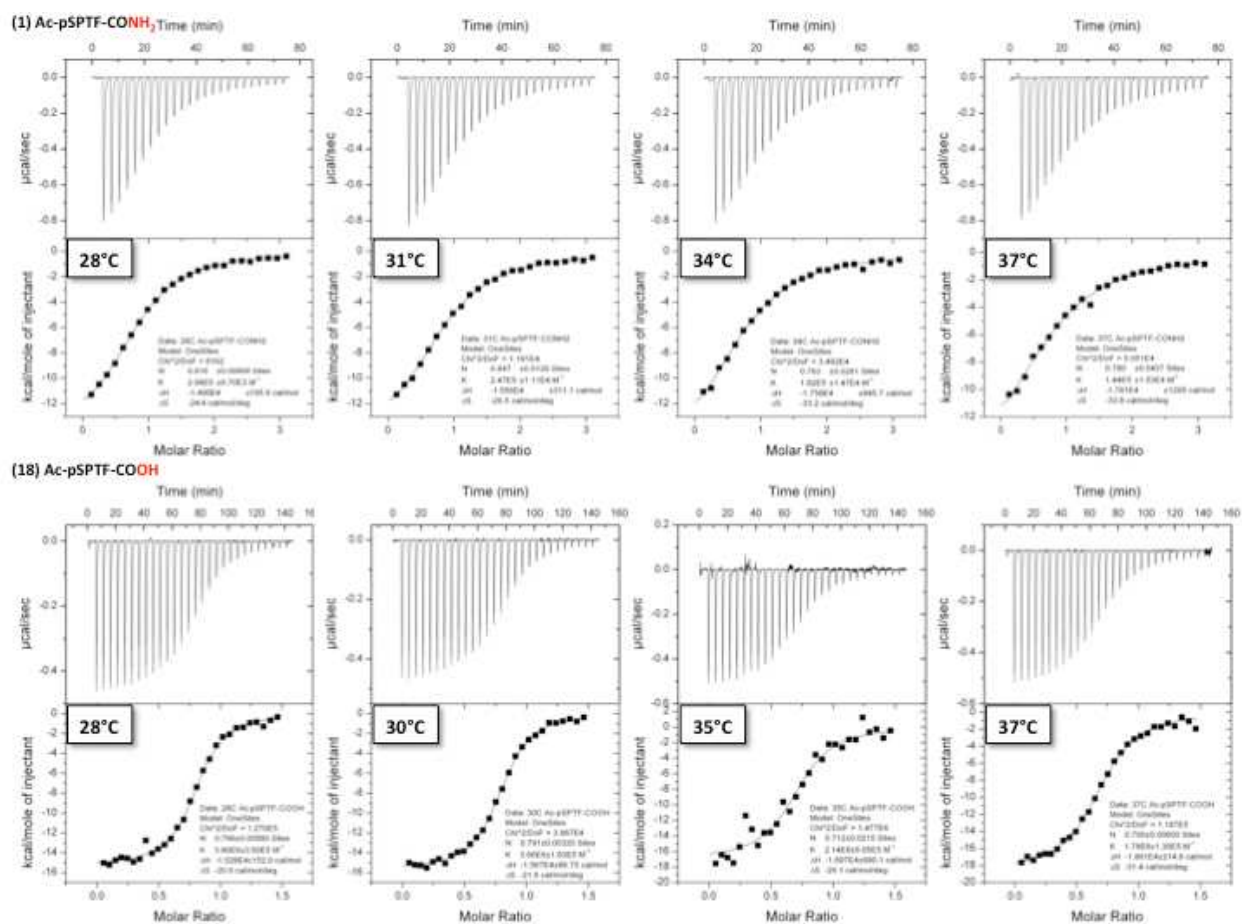


Figure S4. Binding isotherms of the BRCT(BRCA1)-peptide1 and -peptide 18 interaction at various temperatures.

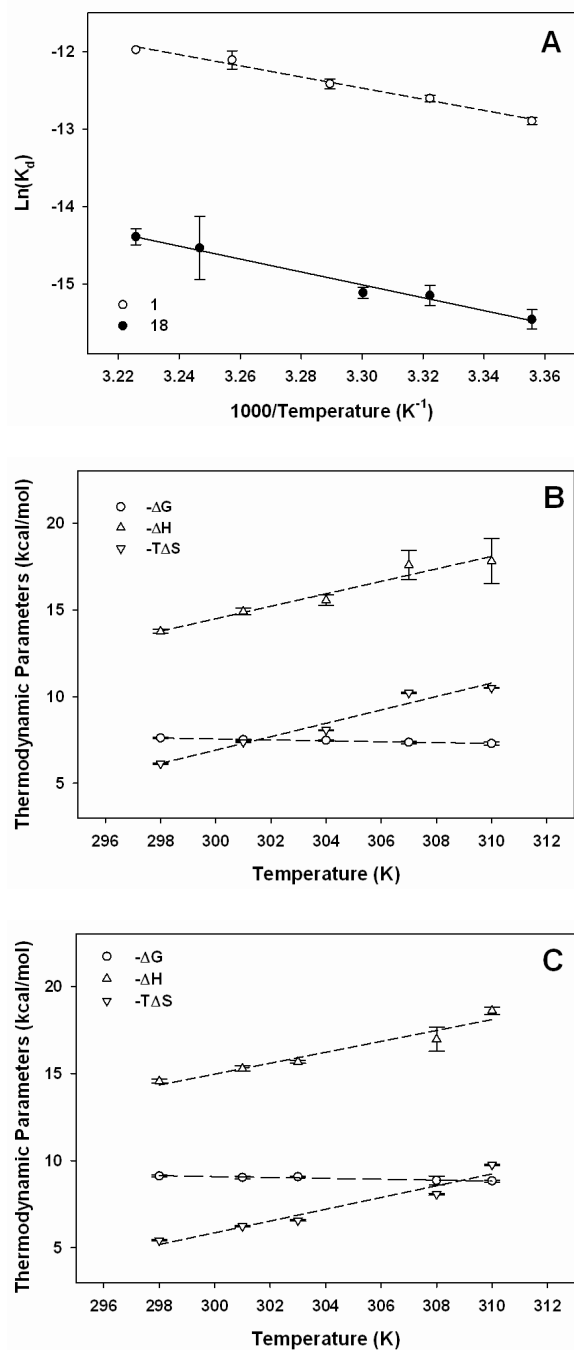


Figure S5. ITC studies to determine the effect of temperature on the thermodynamic parameters of tetrapeptides **1** and **18** binding to BRCT(BRCA1). (A) Linear van't Hoff plots of BRCT(BRCA1) complexed with tetrapeptides **1** (open circles) and **18** (filled circles). The correlation coefficients for **1** and **18** are 0.97 and 0.87 respectively. (B) Tetrapeptide **1** (Ac-pSPTF-CONH₂) binding to BRCT(BRCA1). (C) Tetrapeptide **18** (Ac-pSPTF-CO₂H) binding to BRCT(BRCA1). The ΔG values are shown as open circles, ΔH values are shown as open up triangles and $T\Delta S$ values are shown as open down triangles.