

## *SUPPLEMENTARY MATERIALS*

### **Rational design of novel peptidomimetics against Influenza A virus: biological and computational studies**

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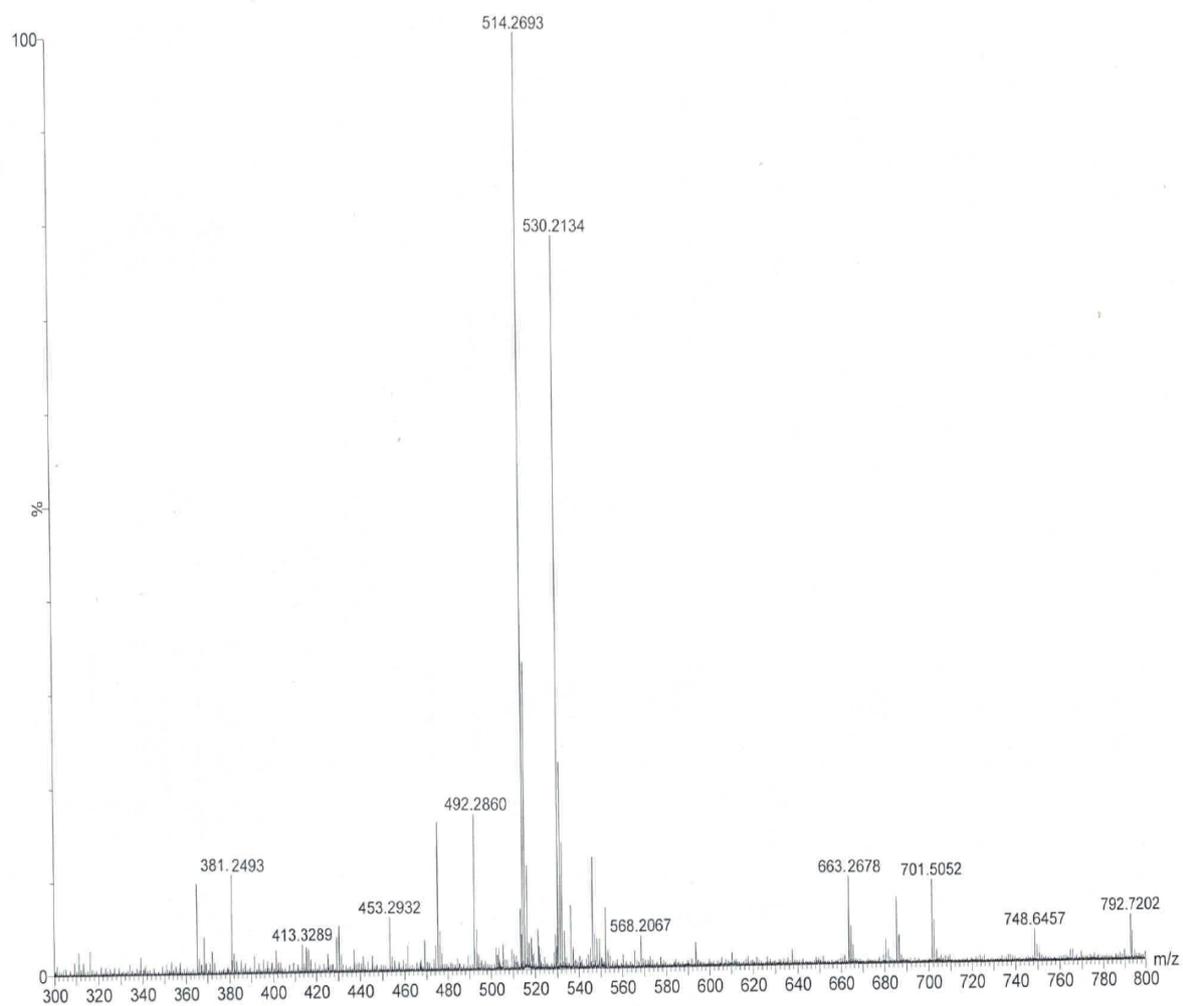
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**Table S1.** Analytical data of peptides **3-18**.

<b>Pep.</b>	<b>Sequence</b>	<b>HPLC k'<sup>a</sup></b>	<b>HRMS</b>
<b>1<sup>b</sup></b>	SLDC	3.93	477.18970
<b>2<sup>b</sup></b>	SKHS	4.68	499.26235
<b>3</b>	(N-Me)SLDC	8.00	492.2860
<b>4</b>	S(N-Me)LDC	9.33	492.2727
<b>5</b>	SL(N-Me)DC	5.20	493.9463
<b>6</b>	SLD(N-Me)C	10.50	492.9463
<b>7</b>	(N-Me)SKHS	7.88	513.2344
<b>8</b>	S(N-Me)KHS	0.44	513.2260
<b>9</b>	SK(N-Me)HS	0.50	513.2026
<b>10</b>	SKH(N-Me)S	0.58	513.2427
<b>11</b>	MhSLDC	4.55	492.2759
<b>12</b>	SMLDC	4.75	478.1846
<b>13</b>	SLNDC	1.15	478.3001
<b>14</b>	SLDMhC	1.10	493.2882
<b>15</b>	MhSKHS	1.15	513.2335
<b>16</b>	SMKHS	1.40	499.2022
<b>17</b>	SKMHS	2.40	498.9463
<b>18</b>	SKHMhS	1.20	513.2522

<sup>a</sup> k'=[(peptide retention time-solvent retention time)/solvent retention time]; <sup>b</sup> Scala et al. (2017).

## Supplementary figures of Mass spectrometry and HPLC of peptides used in the study



Datafile Name: Peptide 3

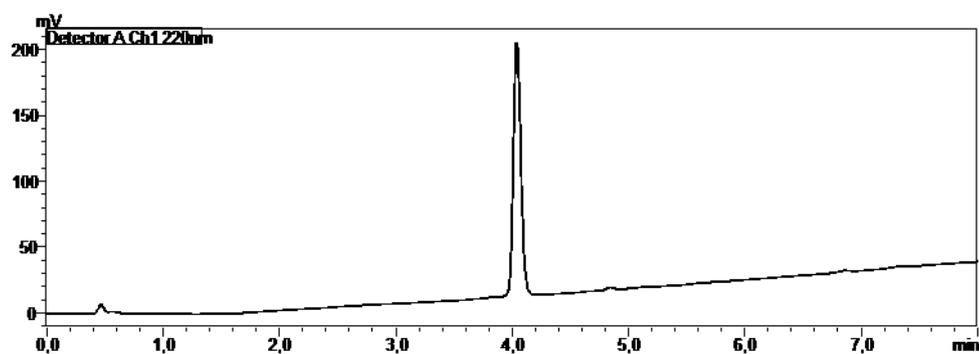
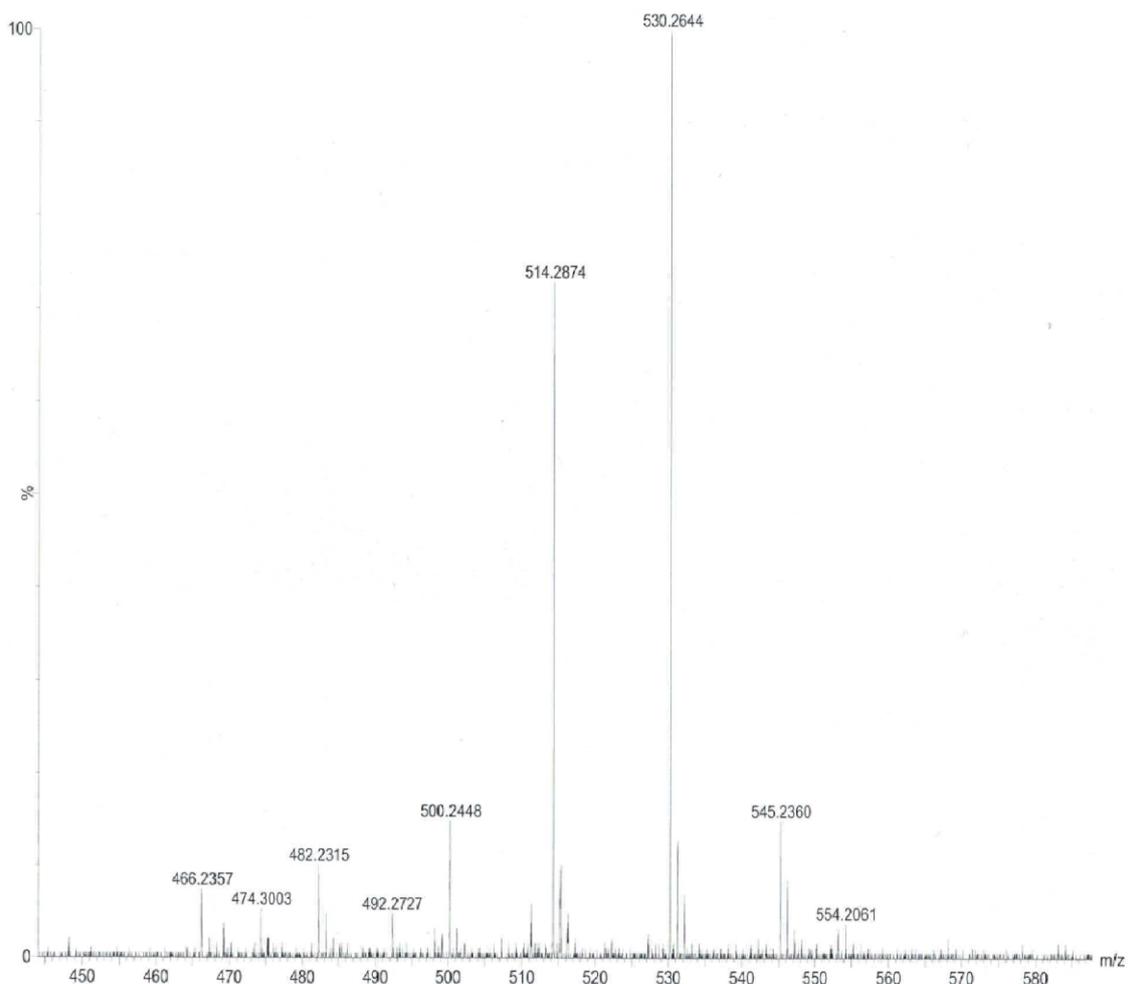


Figure S1. HR-ESI-MS of Peptide 3 ion  $[M+H]^+$  and analytical HPLC trace at 220 nm.



Datafile Name: Peptide 4

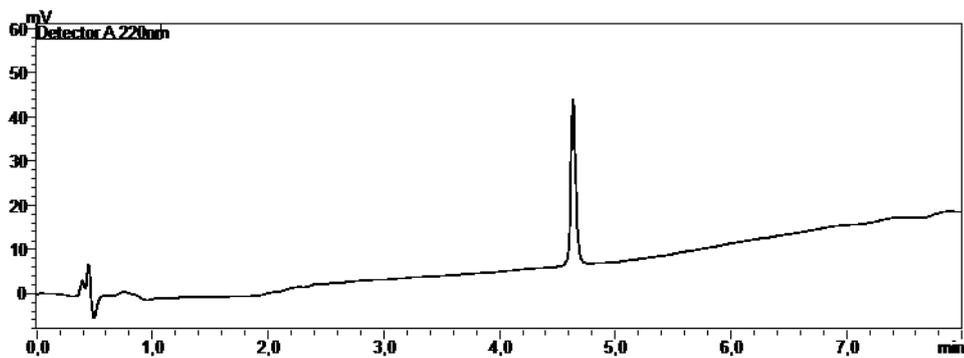
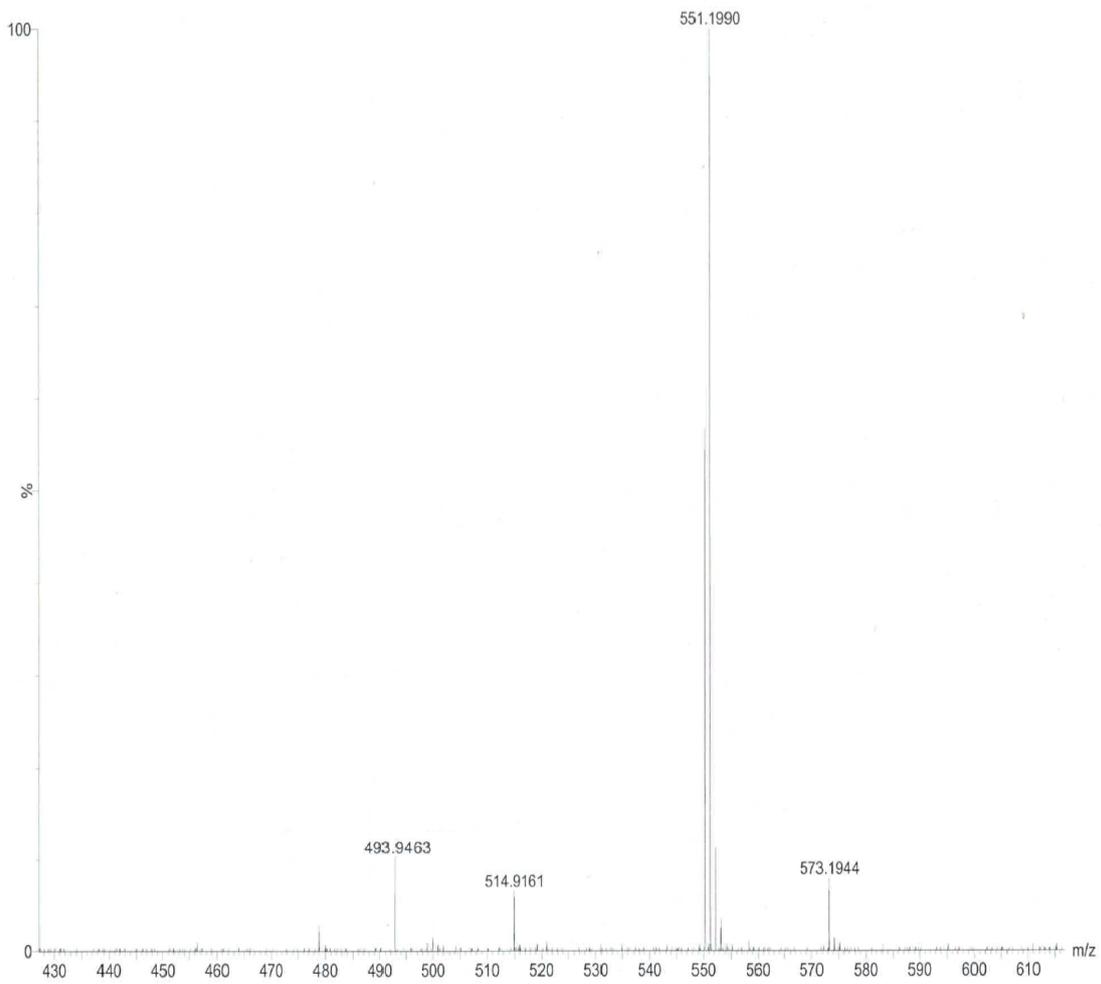


Figure S2. HR-ESI-MS of Peptide 4 ion  $[M+H]^+$  and analytical HPLC trace at 220 nm.



Datafile Name: Peptide 5

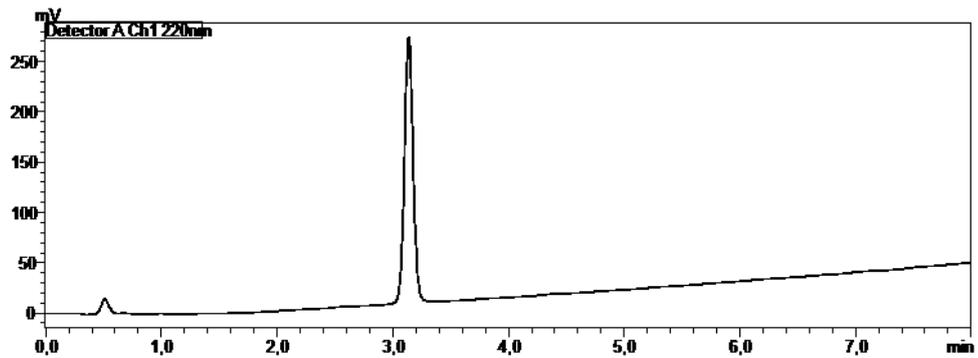


Figure S3. HR-ESI-MS of Peptide 5 ion  $[M+H]^+$  and analytical HPLC trace at 220 nm.

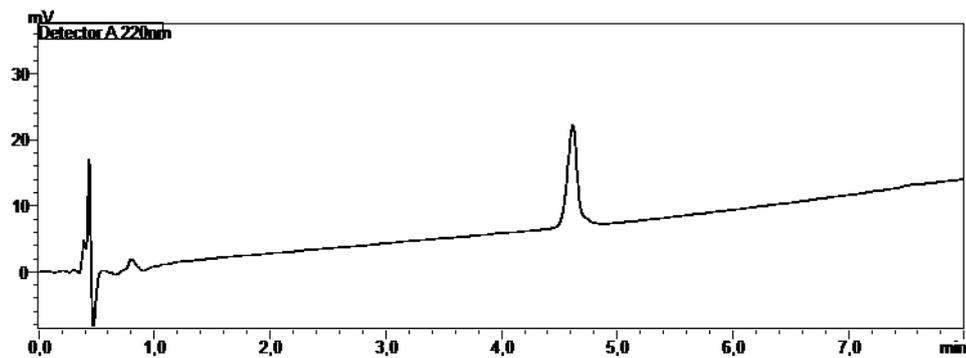
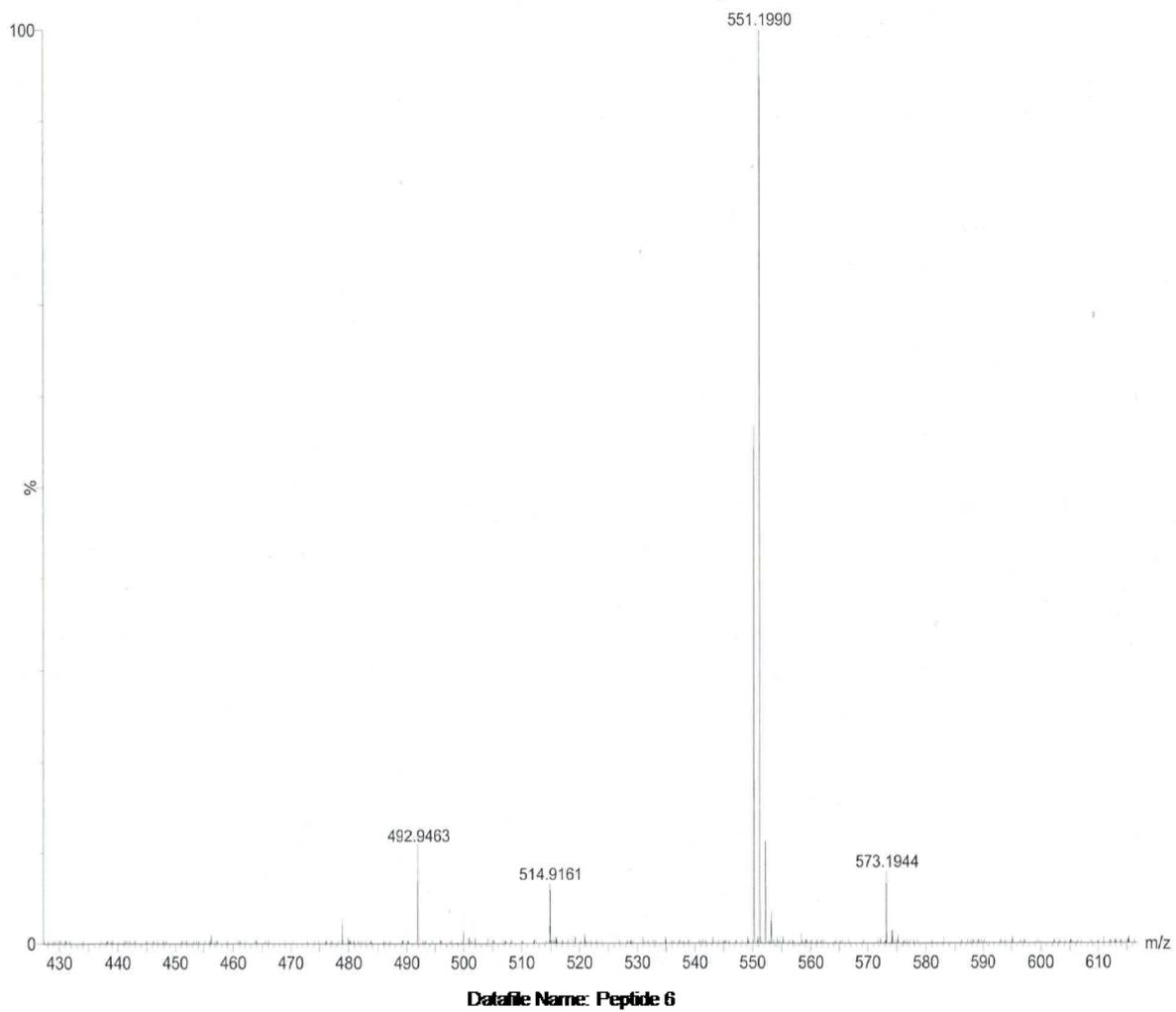
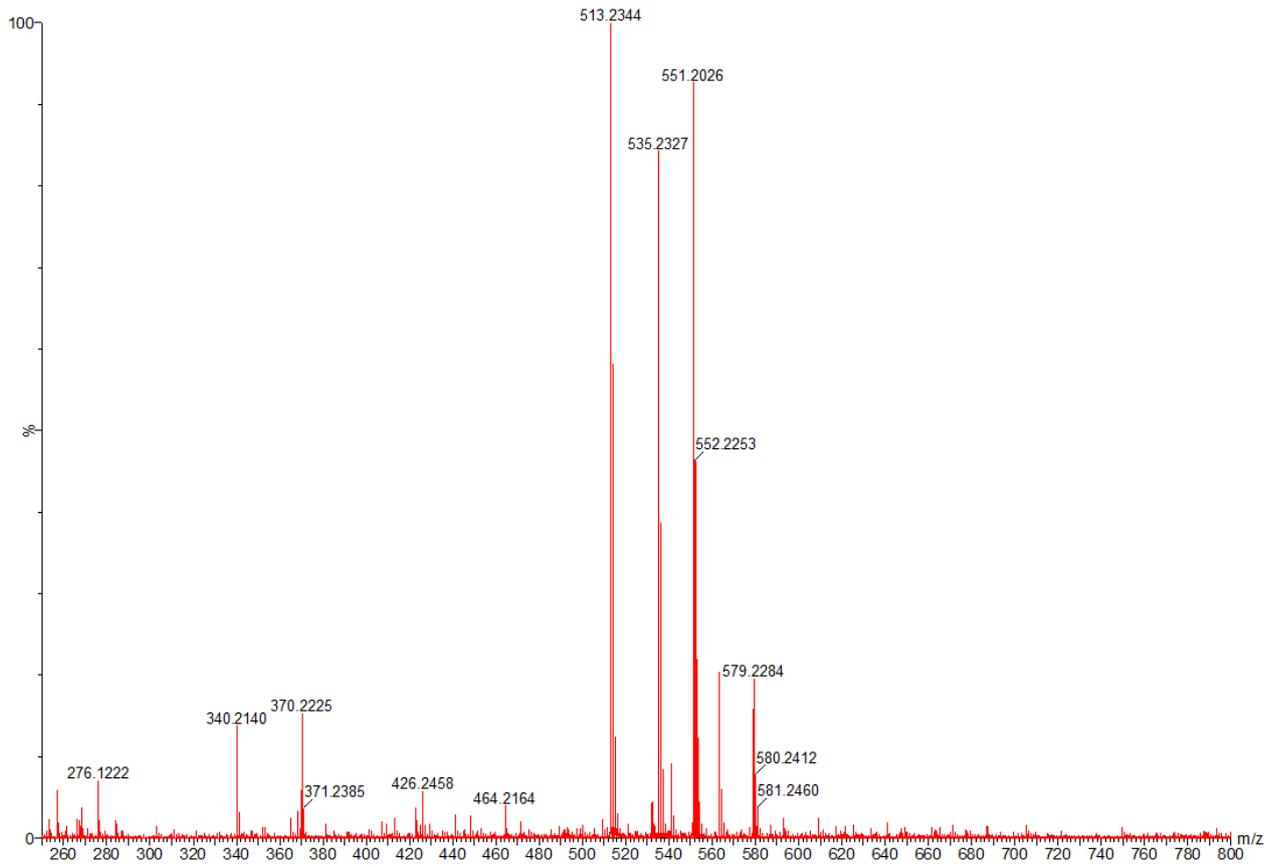


Figure S4. HR-ESI-MS of Peptide 6 ion  $[M+H]^+$  and analytical HPLC trace at 220 nm.



Datafile Name: Peptide 7

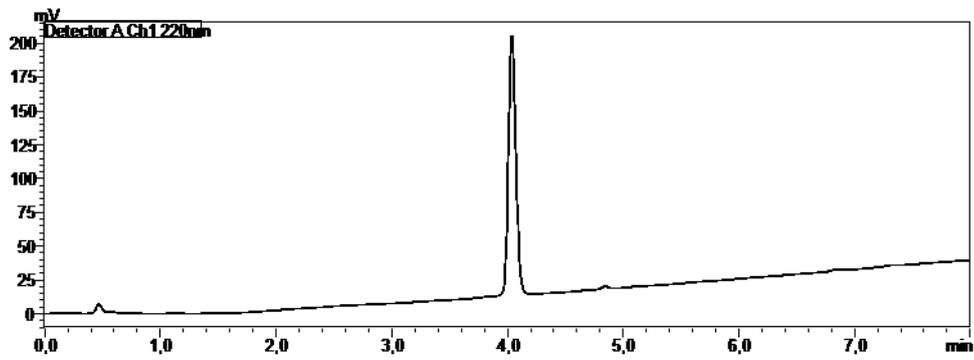
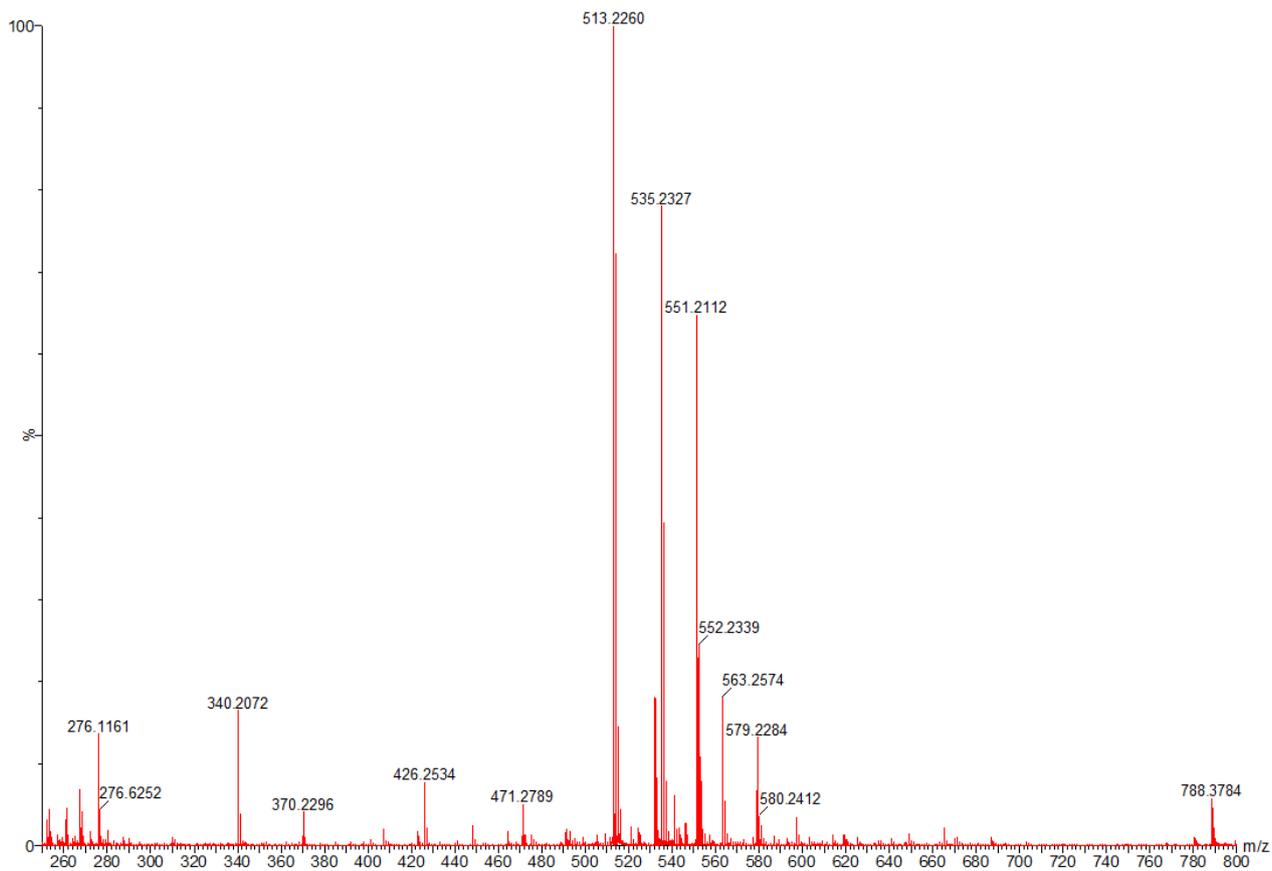


Figure S5. HR-ESI-MS of Peptide 7 ion  $[M+H]^+$  and analytical HPLC trace at 220 nm.



Datafile Name: Peptide 8

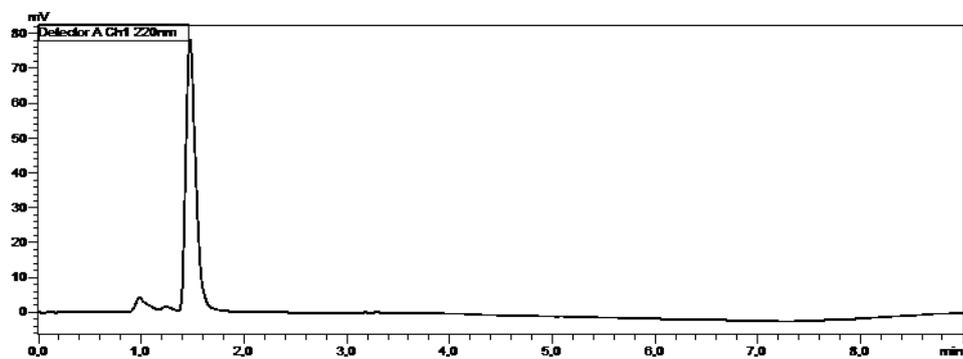
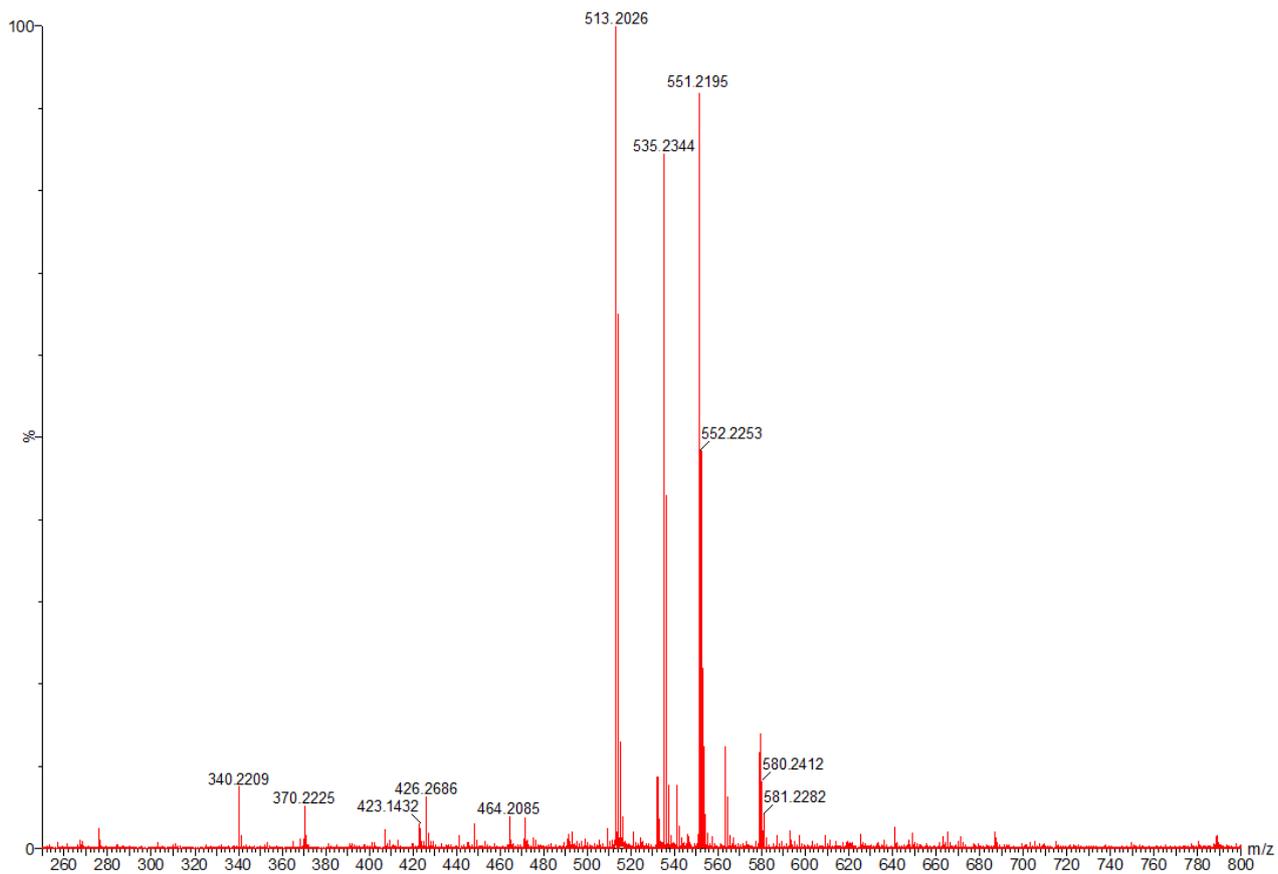


Figure S6. HR-ESI-MS of Peptide 8 ion  $[M+H]^+$  and analytical HPLC trace at 220 nm.



Datafile Name: Peptide 9

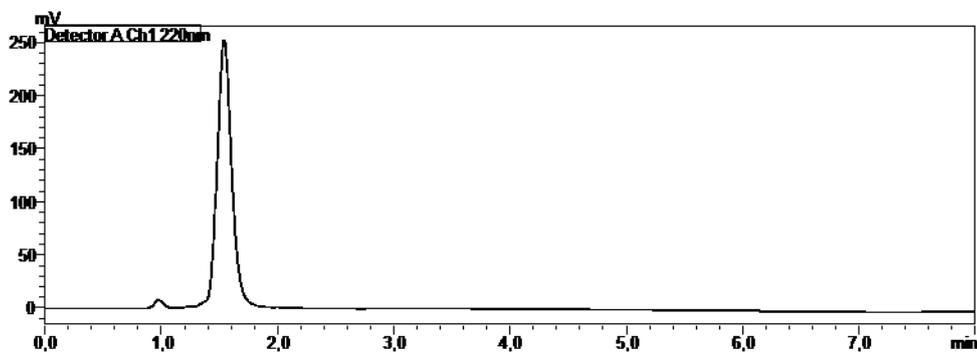
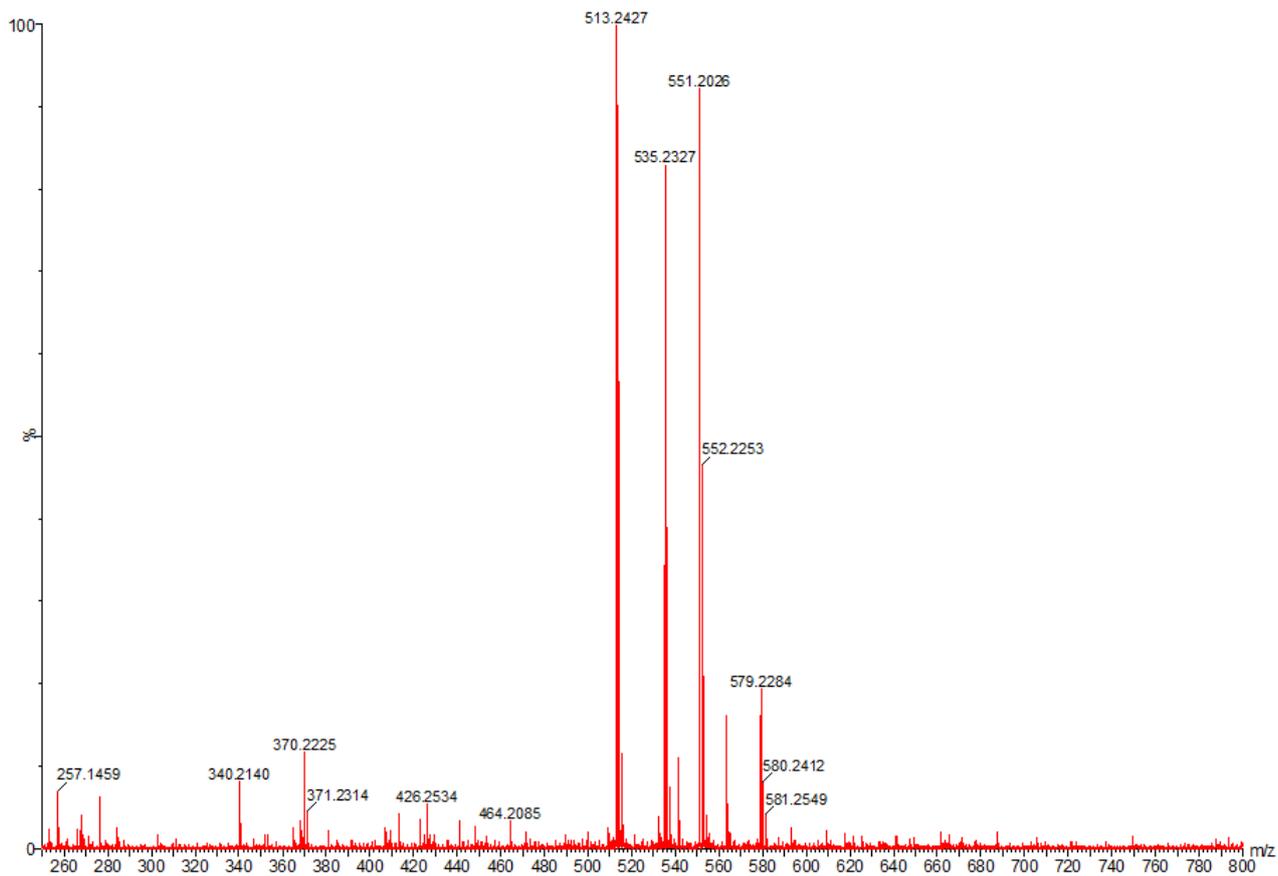


Figure S7. HR-ESI-MS of Peptide 9 ion  $[M+H]^+$  and analytical HPLC trace at 220 nm.



Datafile Name: Peptide 10

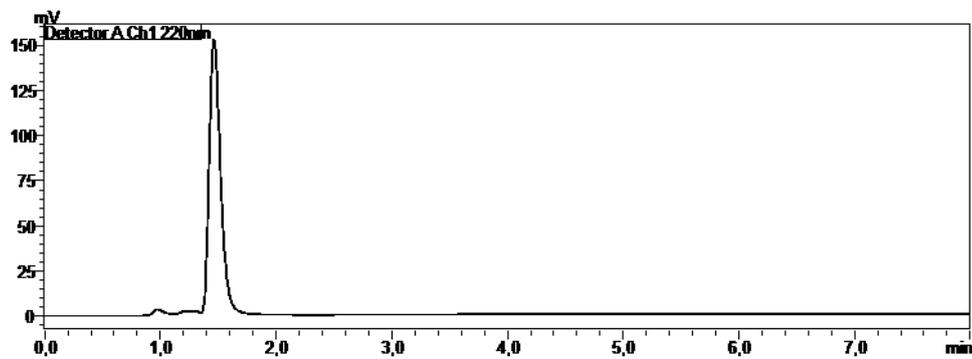
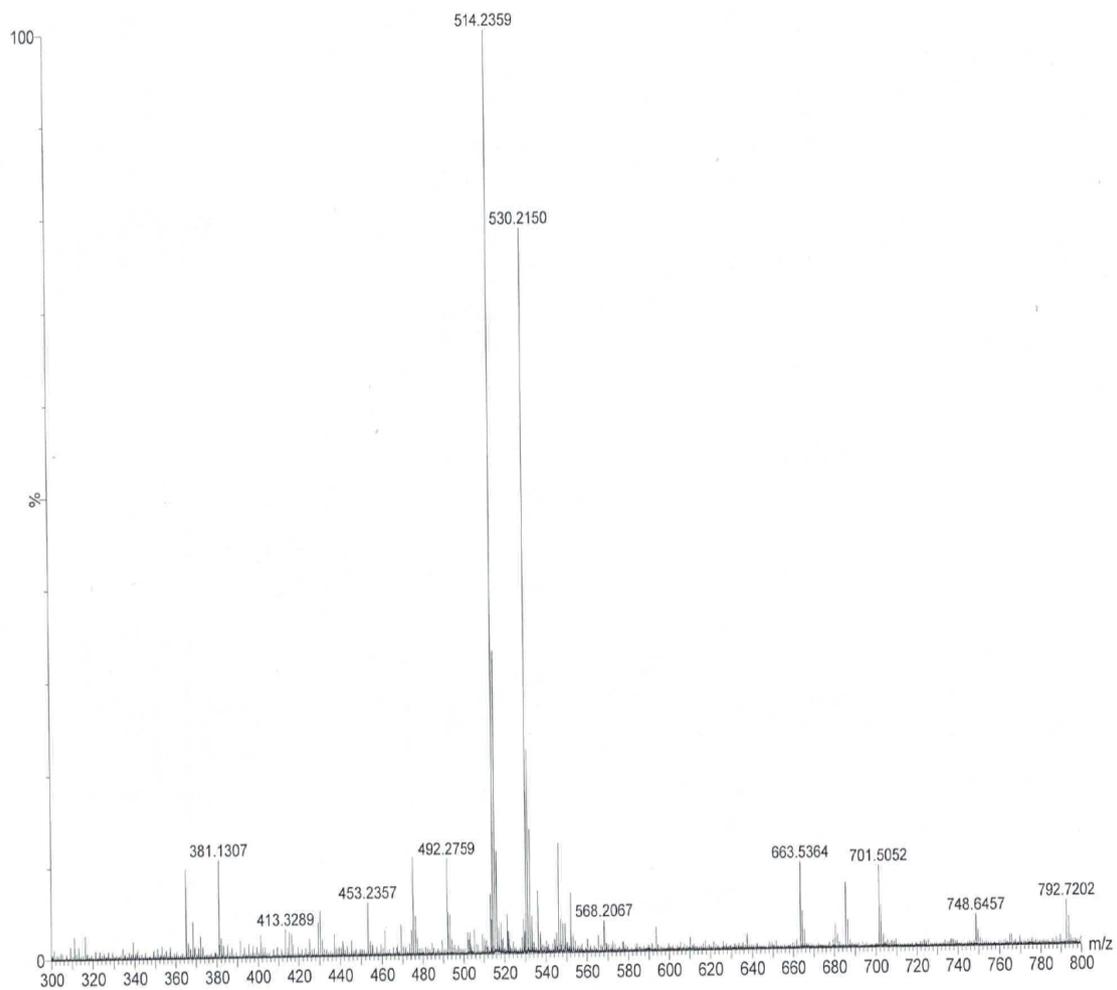


Figure S8. HR-ESI-MS of Peptide 10 ion  $[M+H]^+$  and analytical HPLC trace at 220 nm.



Datafile Name: Peptide 11

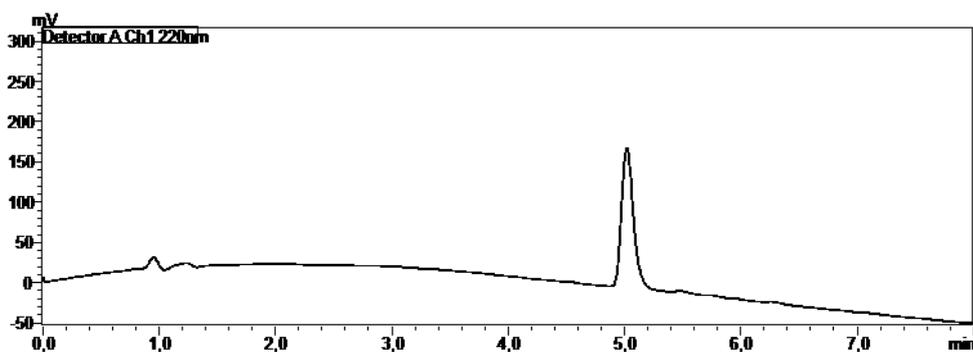
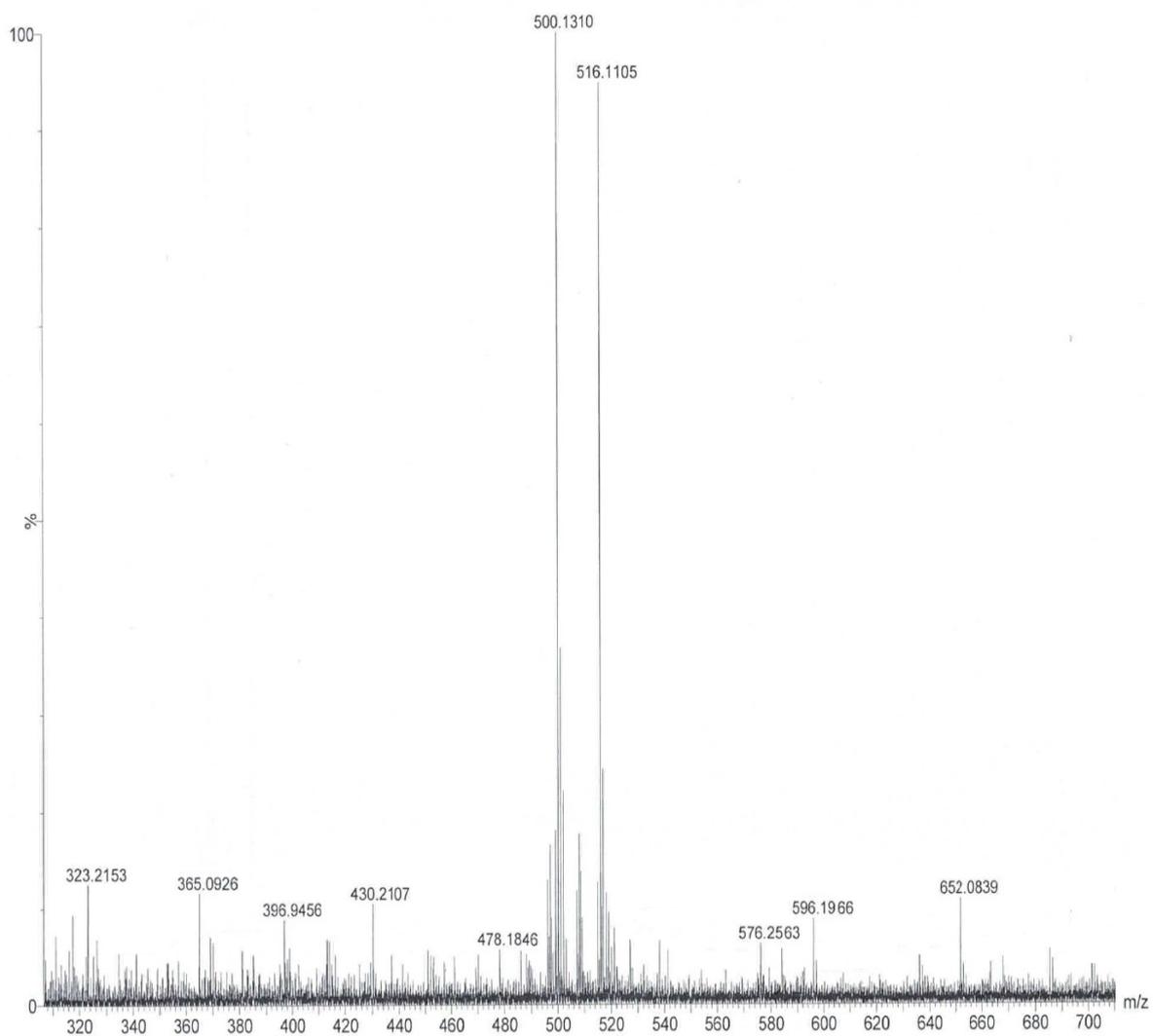


Figure S9. HR-ESI-MS of Peptide 11 ion  $[M+H]^+$  and analytical HPLC trace at 220 nm.



Datafile Name: Peptide 12

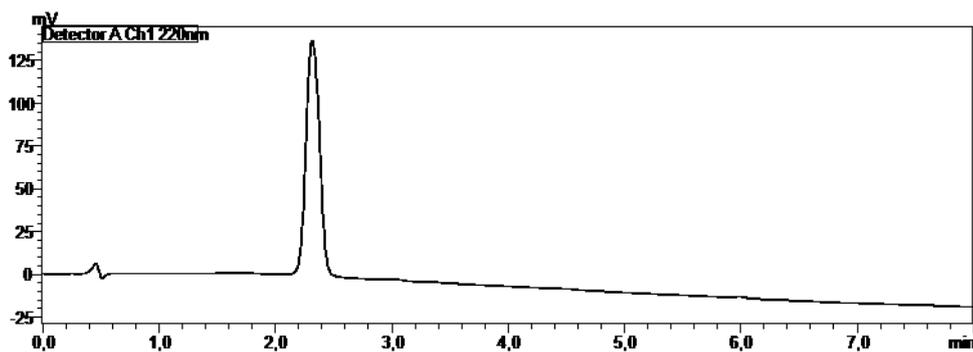
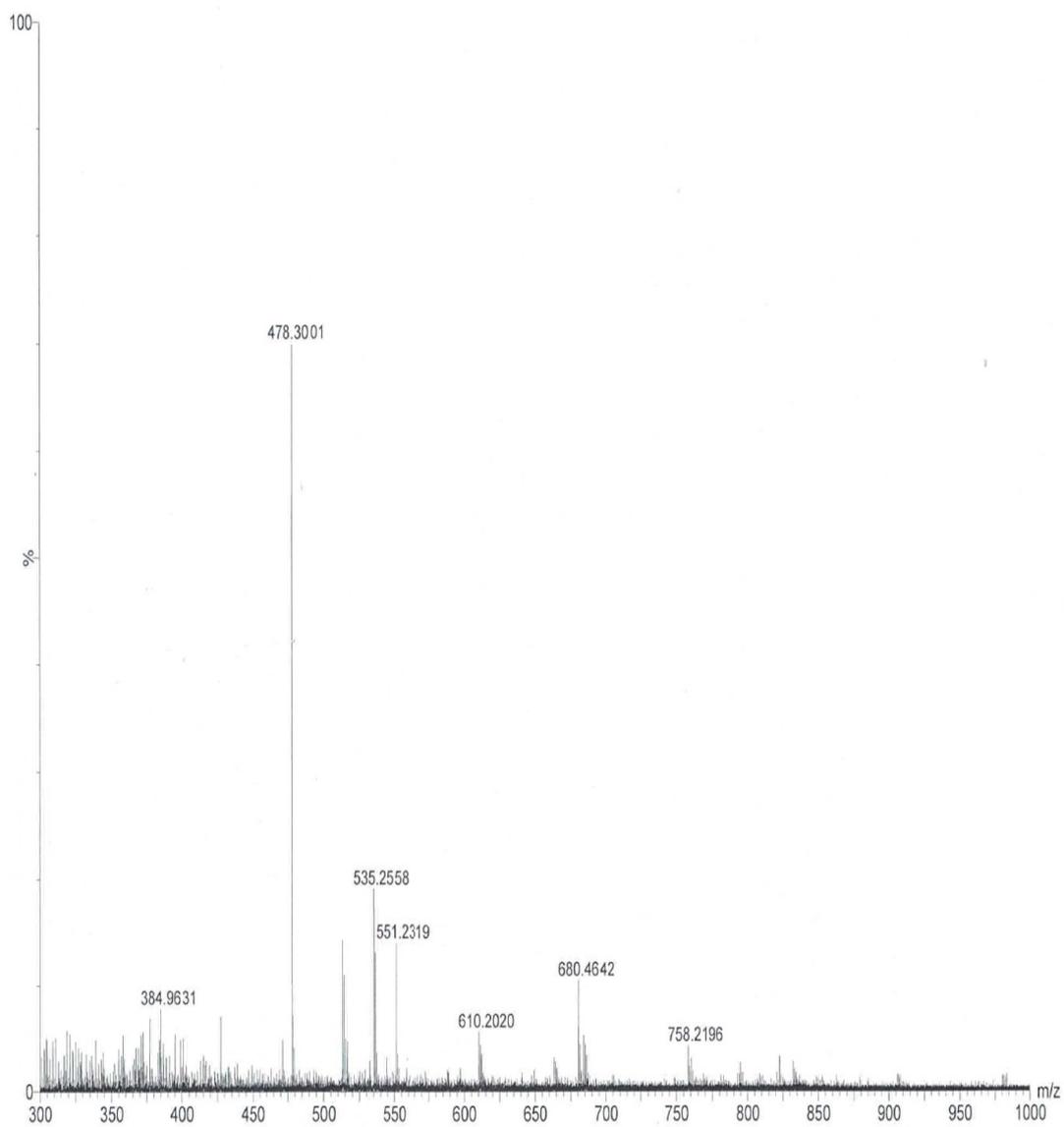


Figure S10. HR-ESI-MS of Peptide 12 ion  $[M+H]^+$  and analytical HPLC trace at 220 nm.



Datafile Name: Peptide 13

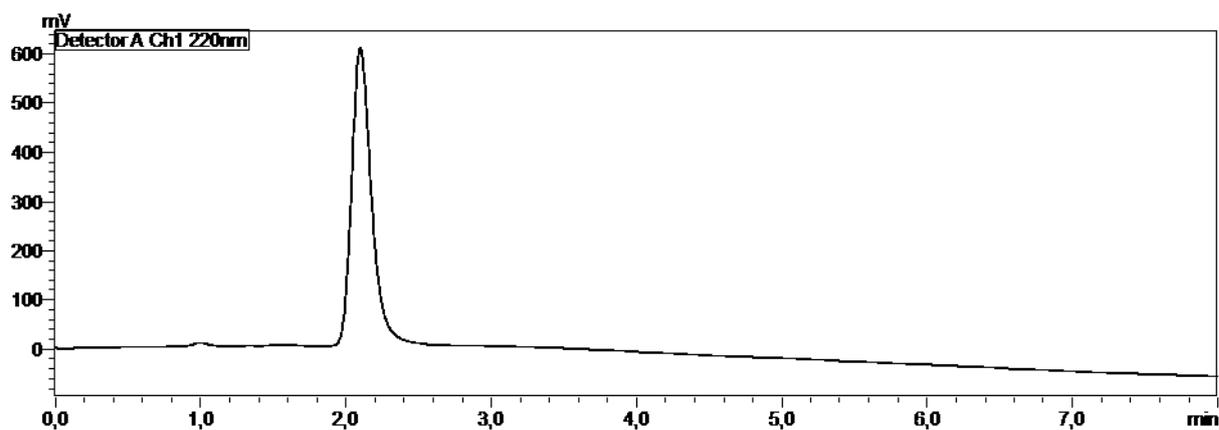
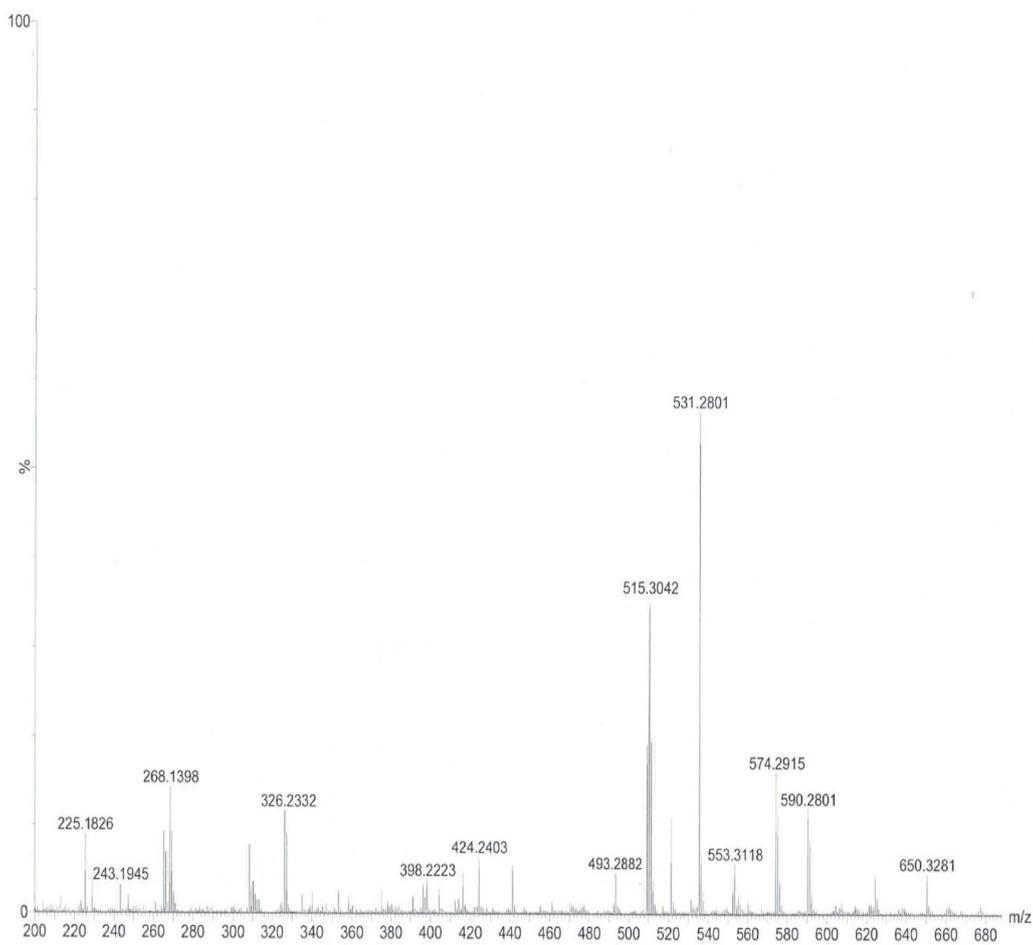


Figure S11. HR-ESI-MS of Peptide 13 ion  $[M+H]^+$  and analytical HPLC trace at 220 nm.



Datafile Name: Peptide 14

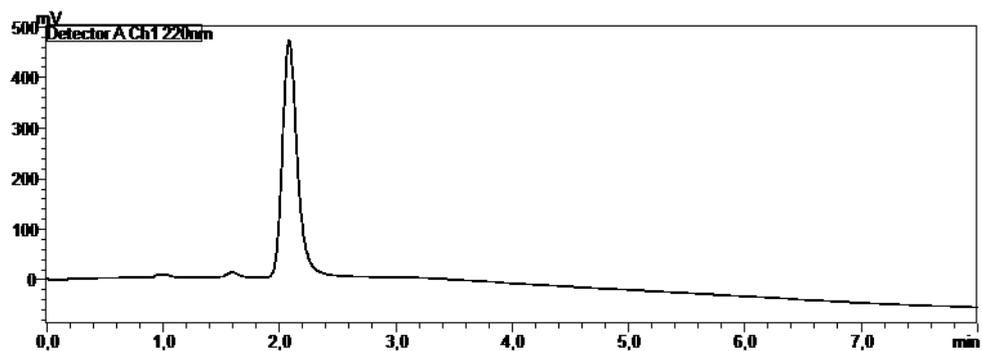


Figure S12. HR-ESI-MS of Peptide 14 ion  $[M+H]^+$  and analytical HPLC trace at 220 nm.

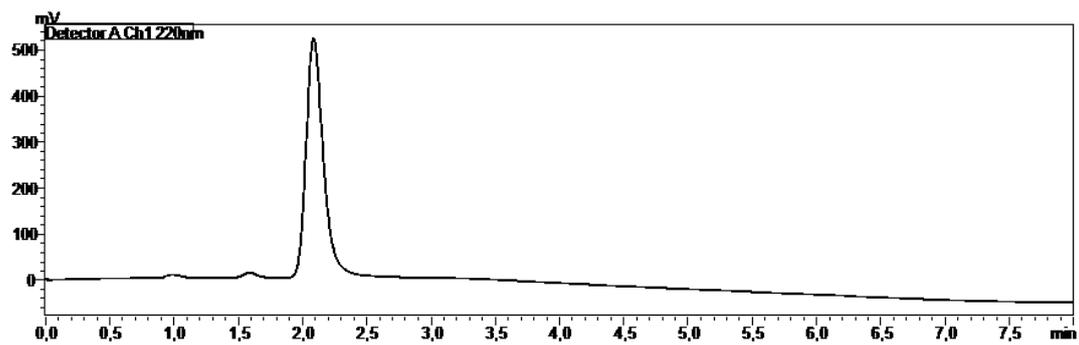
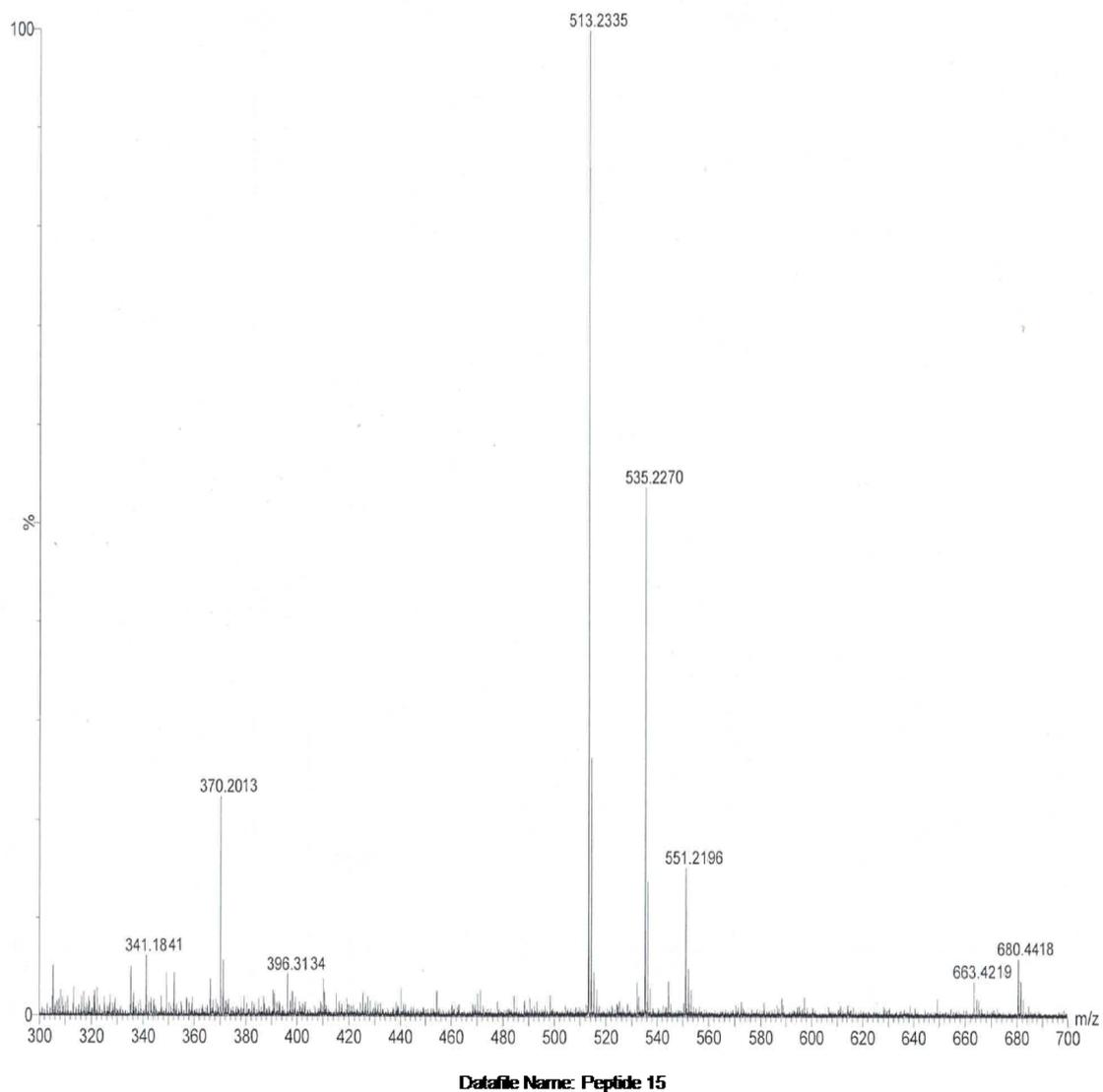


Figure S13. HR-ESI-MS of Peptide 15 ion  $[M+H]^+$  and analytical HPLC trace at 220 nm.

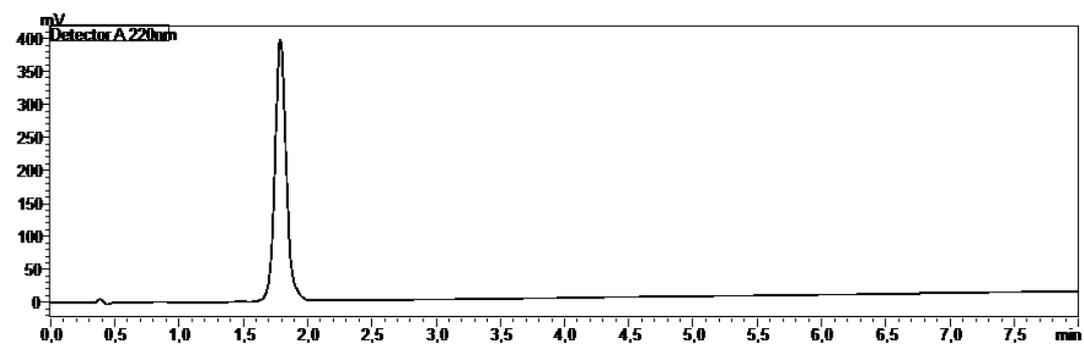
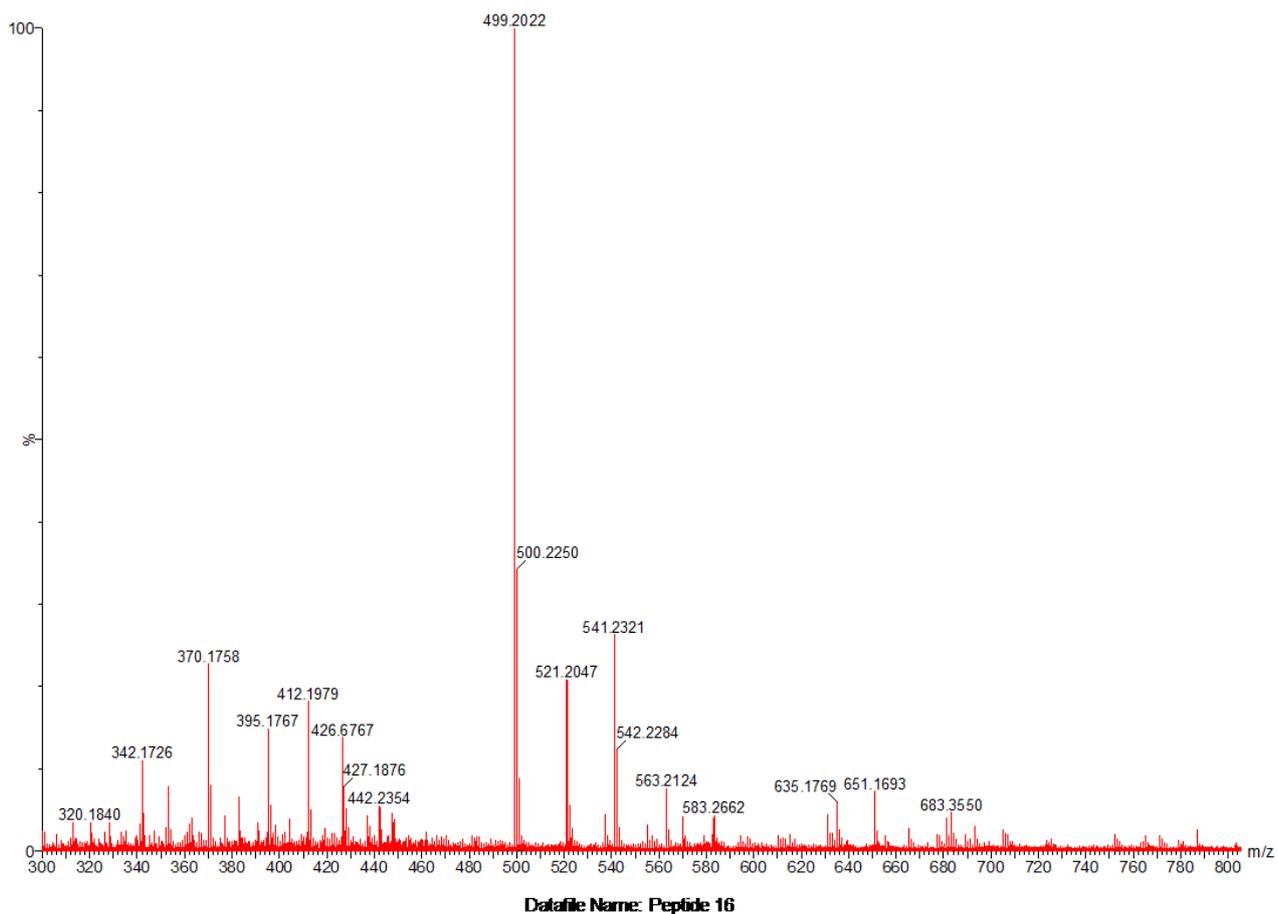


Figure S14. HR-ESI-MS of Peptide 16 ion  $[M+H]^+$  and analytical HPLC trace at 220 nm.

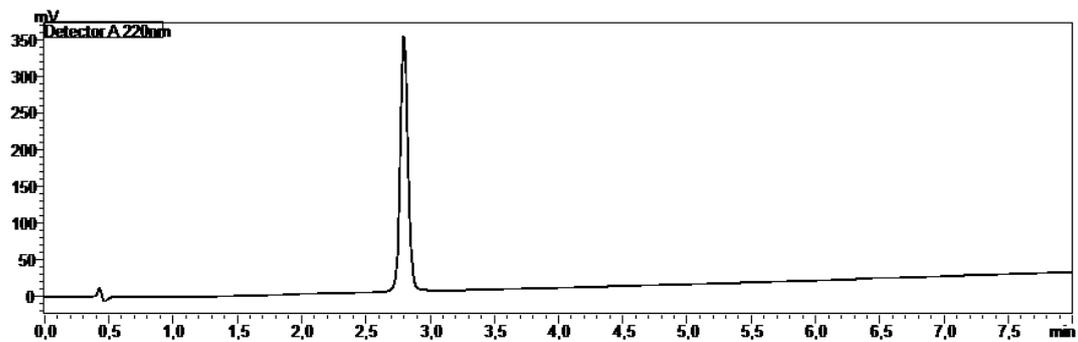
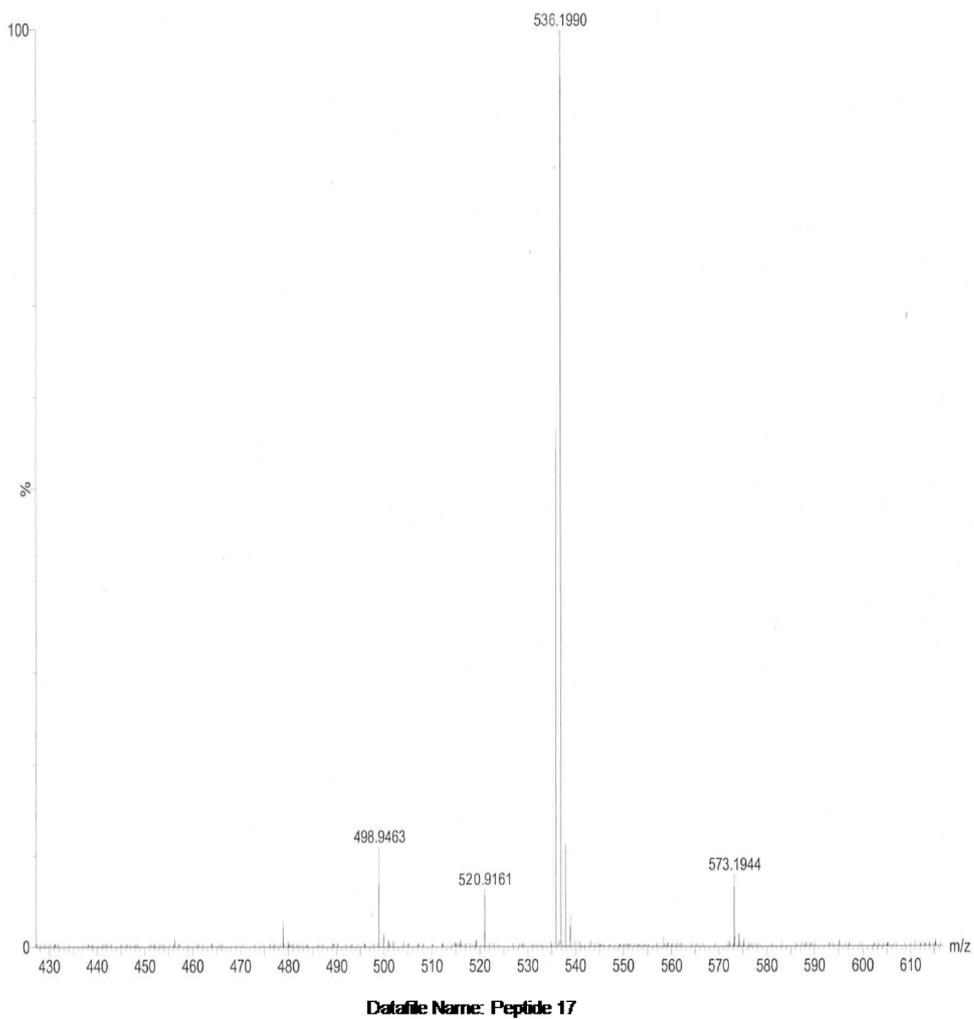


Figure S15. HR-ESI-MS of Peptide 17 ion  $[M+H]^+$  and analytical HPLC trace at 220 nm.

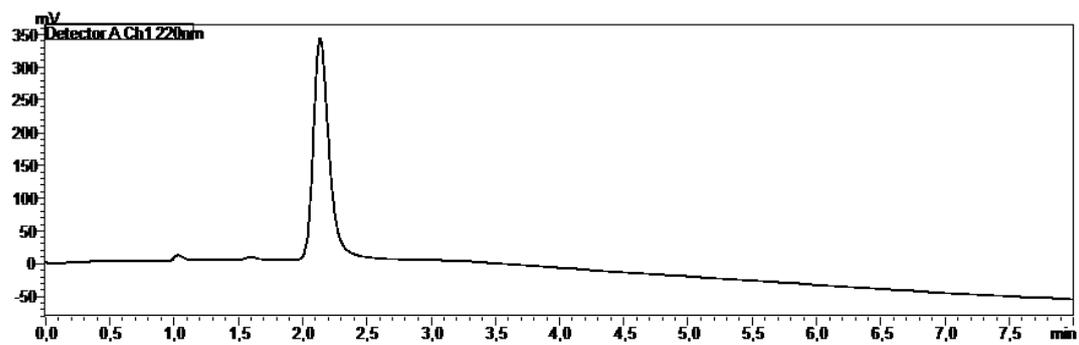
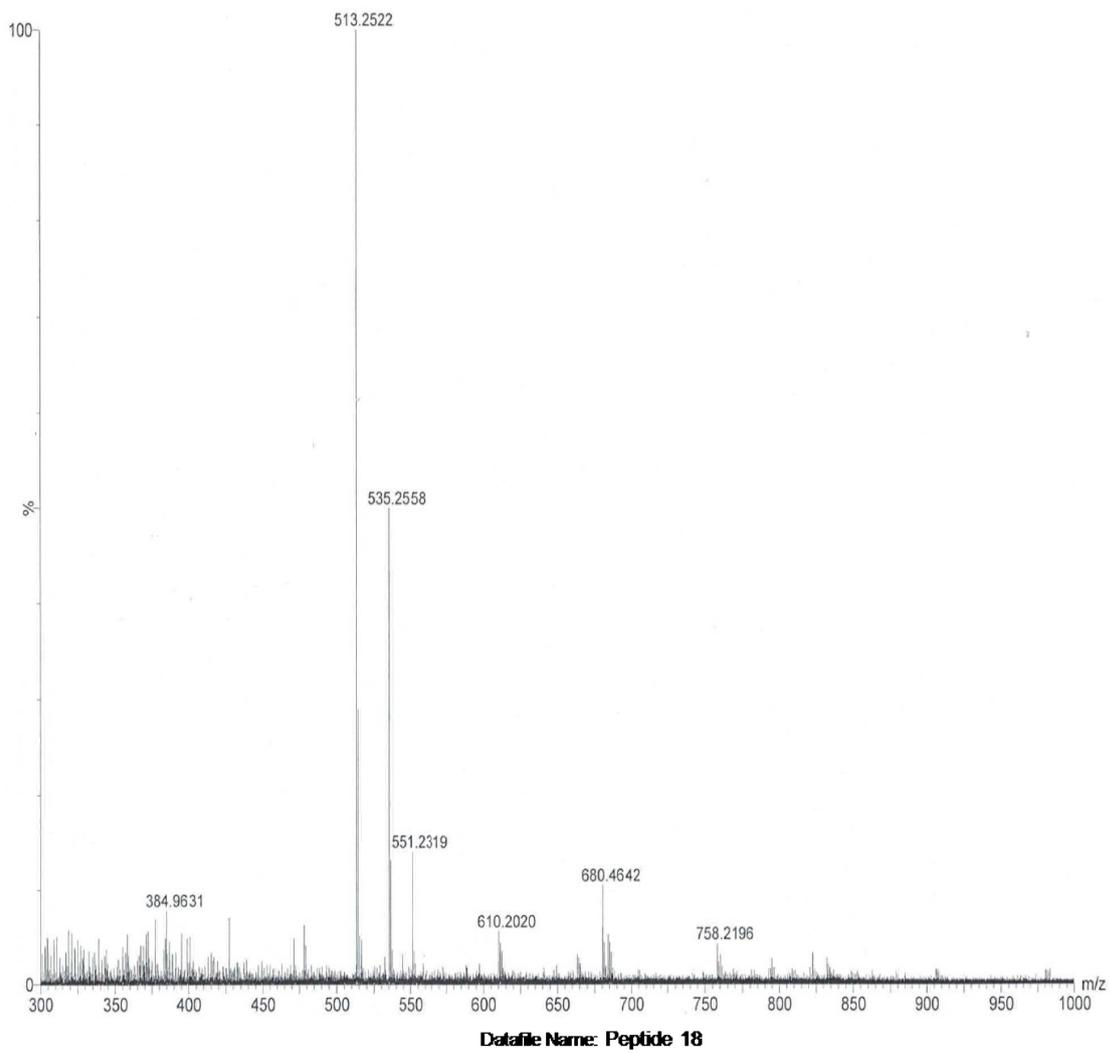
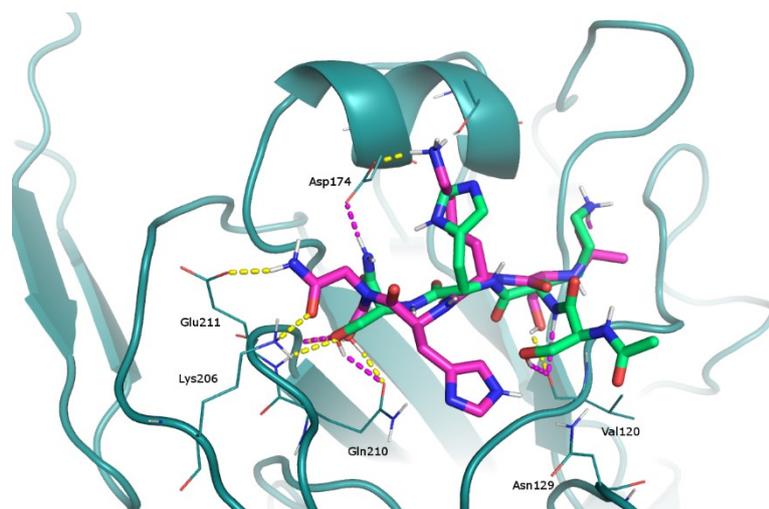
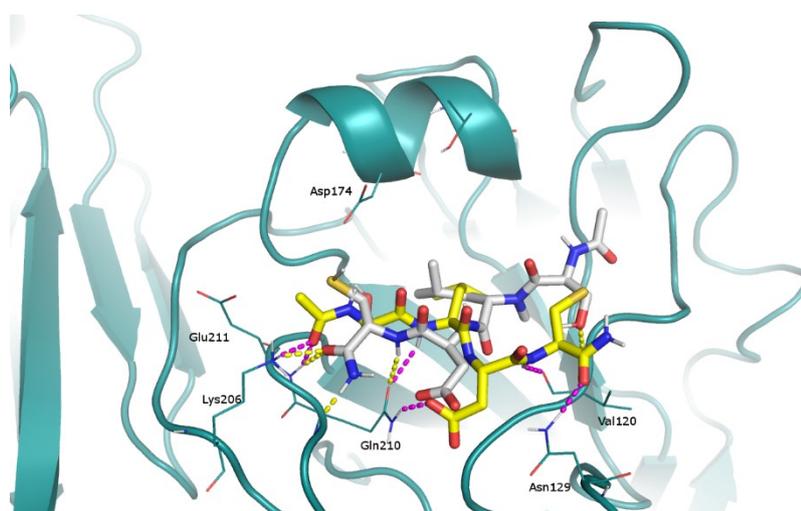


Figure S16. HR-ESI-MS of Peptide 18 ion  $[M+H]^+$  and analytical HPLC trace at 220 nm.



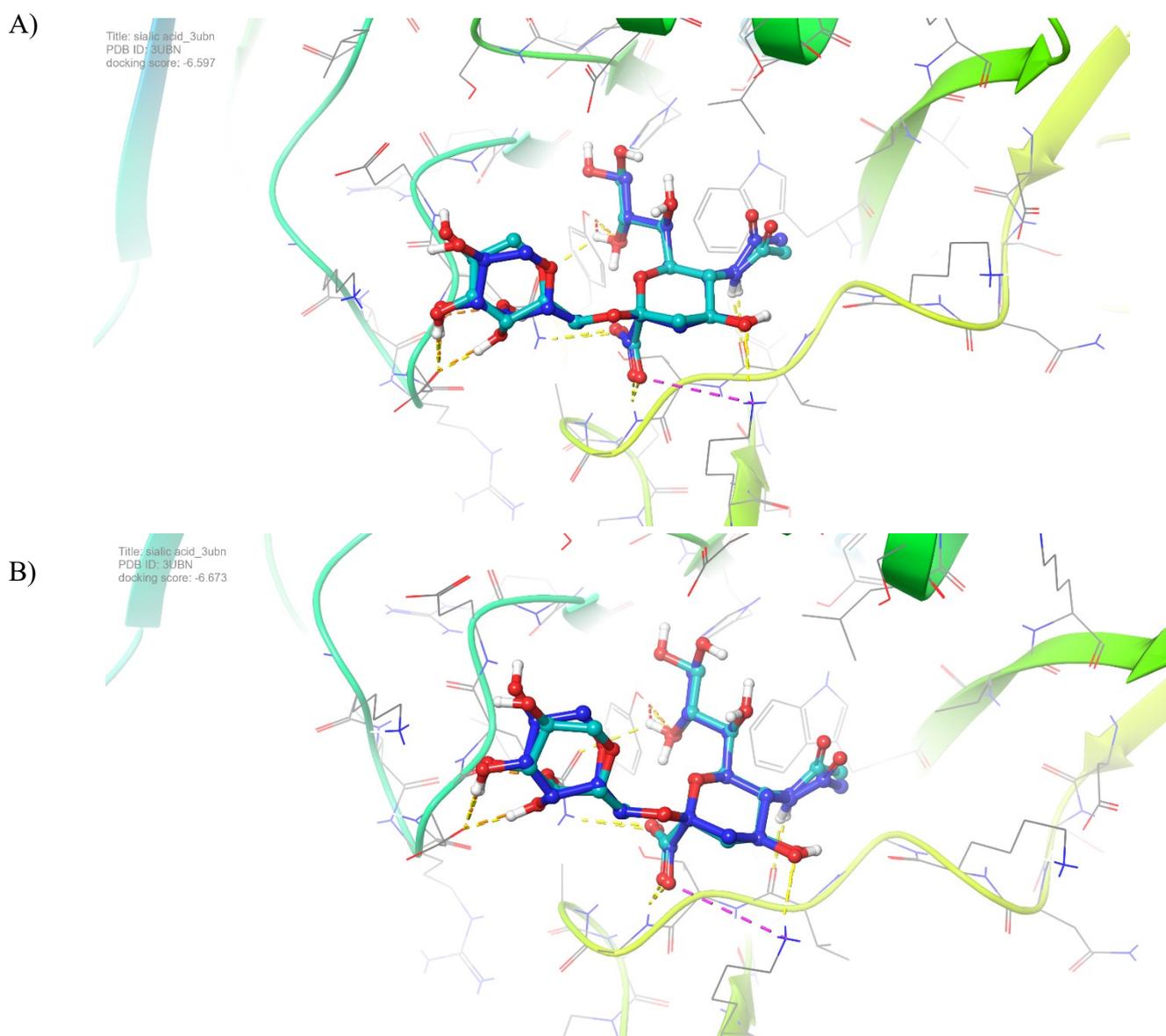
**Figure S17.** Superimposition of the docked poses of peptoid **18** and reference tetrapeptide **2** represented as sticks (magenta and green C atoms, respectively) in the RBS of A/Parma/24/09 H1N1 (deep-cyan cartoon). Just the HA residues that interact with the ligands are shown as lines for clarity's sake. H-bonds are represented as yellow dashed lines for ligand **18** and magenta for ligand **2**.



**Figure S18.** Superimposition of the docked poses of N-methyl peptides **4** and reference tetrapeptide **1** represented as sticks (white and yellow C atoms, respectively) in the RBS of A/Parma/24/09 H1N1 (deep-cyan cartoon). Just the HA residues that interact with the ligands are shown as lines for clarity's sake. H-bonds are represented as yellow dashed lines for ligand **4** and magenta for ligand **1**.

To assess the validity of the docking protocol, the X-ray ligand 6'-sialyl-N-acetylglucosamine was redocked in the receptor binding site of the H1 HA (PDB ID: 3UBN, Proc. Natl. Acad. Sci. USA **2018**, 115, 4240–4245).

Both Glide SP-peptide and Glide SP docking protocols were applied obtaining comparable results. The RMSD calculated superimposing the crystallographic and docked poses are 0.86 and 0.81, and obtained docking score values are -6.597 and -6.673 with Glide SP-peptide and Glide SP, respectively. (Figure S19)



**Figure S19.** 6'-sialyl-N-acetylglucosamine in its X-ray geometry (blue C atoms), superimposed to its best docked pose (cyan C atoms) obtained with the Glide SP-peptide (panel A) and Glide SP docking protocol (panel B). H-bonds and ionic contacts are represented respectively as yellow and purple dashed lines; the docking score value is reported in the high left corner.