Supplementary Information

Table S1. Chemical shifts (ppm) of PepE evaluated at 600 MHz and 298 K.

Residue	H_N	H_α	H_β	H_γ	Others
♦ 1Y		4.23	3.13		Hδ 7.16 Hε 6.88
2G	8.56	3.98 3.82			
3E	8.46	4.33	2.08 1.97	2.42	
4C	8.47	4.77	2.94 2.87		
5P		4.45	2.30	2.03 1.96	Hδ 3.77
6C	8.38	4.49	2.94		
7Allyl-E	8.58	4.48	2.22 2.02	2.46	Allyl group 5.96, 5.36, 5.30, 4.75

♦ Amino acids are indicated by the one letter codes preceded by sequence number.

Table S2. Chemical shifts (ppm) of PepK evaluated at 600 MHz and 298 K.

Residue	H_N	H_α	H_β	H_γ	Others
♦ 1Y		4.24	3.13		Hδ 7.16, 7.11 Hε 6.88, 6.84
2G	8.57	3.98 3.82			
3E	8.50	4.32	2.04 1.96	2.39	
4C	8.53	4.78	2.91		
5P		4.45	2.30	2.02 1.95	Hδ 3.78
6C	8.39	4.49	2.93		
7Allyl-K	8.61	4.42	1.94 1.80	1.45	Hε 2.99 Hδ 1.68 Hζ 7.53 Allyl 5.95, 5.34, 5.28, 4.67

♦ Amino acids are indicated by the one letter codes preceded by sequence number.

Table S3. Chemical shift deviations of H_α protons from random coil values (CSD) for PepE [24]. The CSD value for Allyl-E (residue number 7) is not shown due to the lack of a tabulated random coil value for the modified amino-acid. For Gly average H_α chemical shift values were taken into accounts.

Residue	$H\alpha_{obs}$	$H\alpha_{randomcoil}$	CSD ($H\alpha_{obs} - H\alpha_{randomcoil}$)
♦ 1Y	4.23	4.43	−0.2
2G	3.98	4.11	0.02
	3.82	3.65	
3E	4.33	4.24	0.09
4C	4.77	4.52	0.25
5P	4.45	4.33	0.12
6C	4.49	4.52	−0.03
7Allyl-E	4.48	–	–

♦ Amino acids are indicated by the one letter codes preceded by sequence number.

Table S4. CSD (*i.e.*, $H\alpha_{obs} - H\alpha_{randomcoil}$) of PepK.

Residue	$H\alpha_{obs}$	$H\alpha_{randomcoil}$	CSD ($H\alpha_{obs} - H\alpha_{randomcoil}$)
♦ 1Y	4.24	4.43	−0.19
2G	3.98	4.11	0.02
	3.82	3.65	
3E	4.32	4.24	0.08
4C	4.78	4.52	0.26
5P	4.45	4.33	0.12
6C	4.49	4.52	−0.03
7Allyl-K	4.42	–	–

♦ Amino acids are indicated by the one letter codes preceded by sequence number.

Table S5. The average number of H-bonds that each residue in PepE and PepK formed with water molecules during MD simulations.

Residue	PepE	PepK
Y	7	8
G	3	2
E	9	6
C	2	1
P	1	3
C	2	4
E or K	9	6

Amino acids are indicated by the one letter codes.

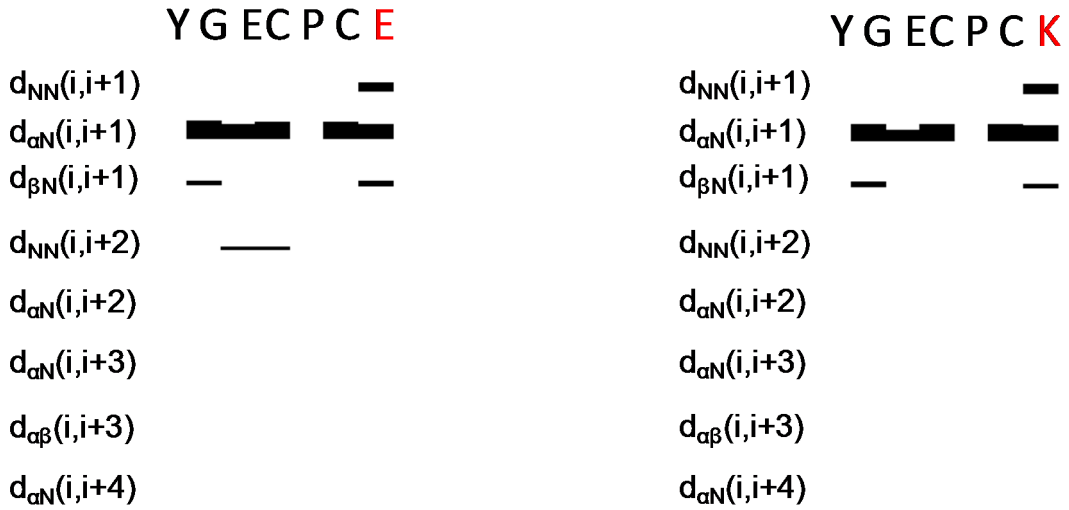

Figure S1. ROE diagrams for PepE (**left**) and PepK (**right**) in H_2O/D_2O (90/10). Peptide sequences are reported on the top; "d_{lm} (i, $i + x$)" indicates a contact between the Hl and Hm protons in the i and $i + x$ residue respectively. The allyl-containing amino acids are highlighted in red.

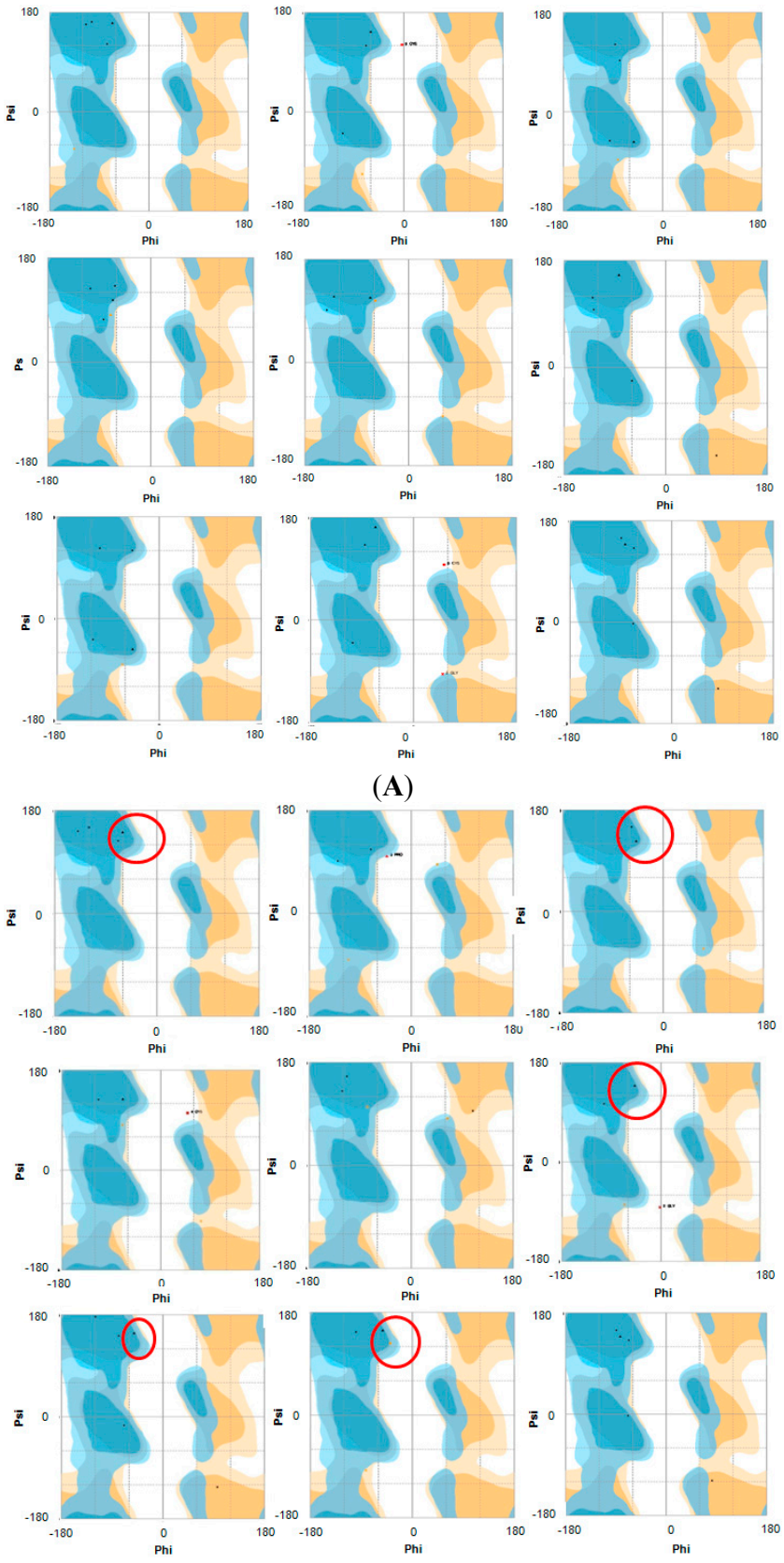

Figure S2. Ramachandran Plot for nine and eight clusters obtained for PepE (**A**) and PepK (**B**), respectively. We indicate by red circle the residues present in the polyproline II region.

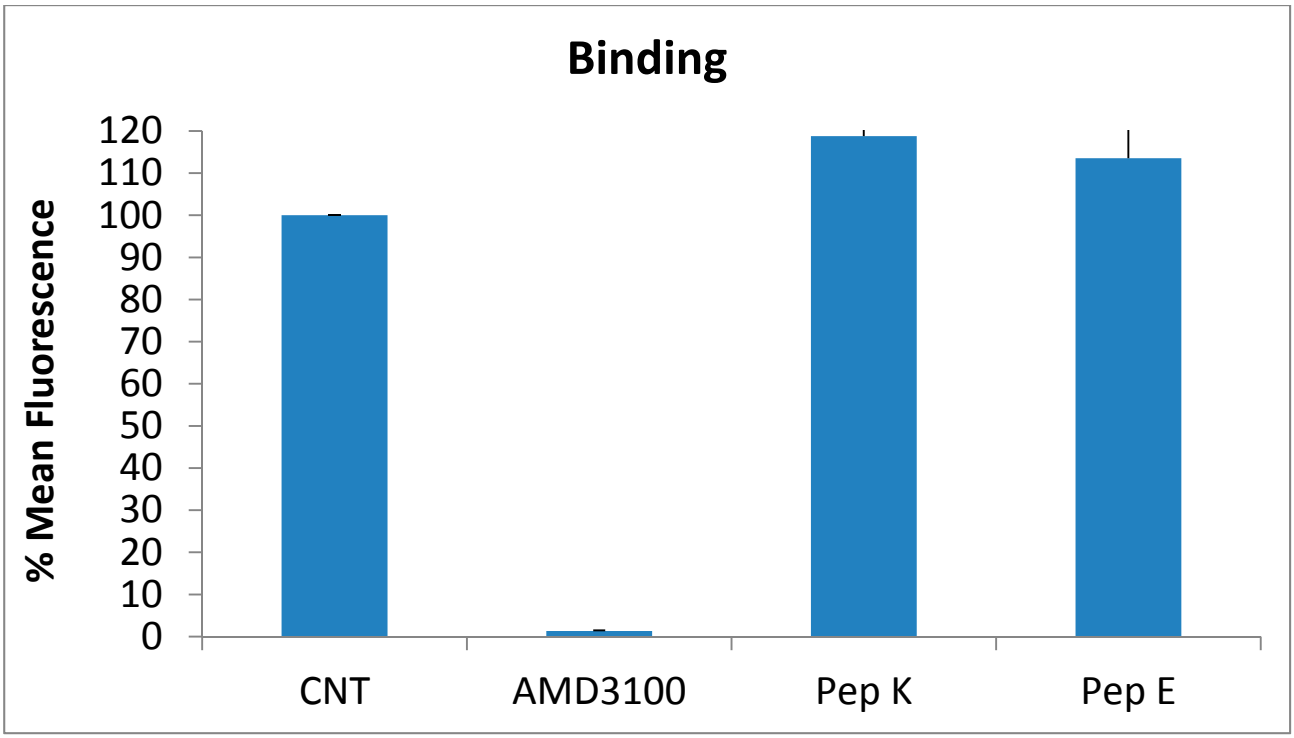

Figure S3. Binding of peptides to CXCR4. The binding was evaluated indirectly through flow cytometry. In particular, histograms indicate the fluorescence percentage for CXCR4 antibody (CNT), AMD3100, PepK and PepE.

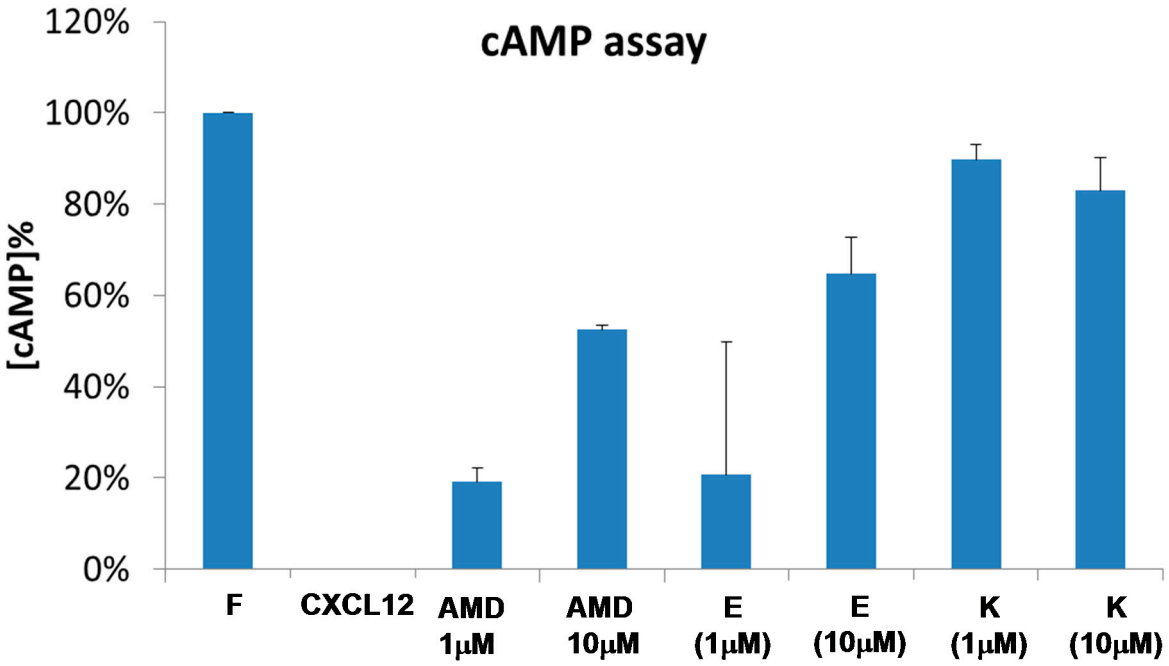

Figure S4. Comparison of inhibition of cAMP modulation by PepE, PepK and AMD3100 at 1 and 10 μM. Briefly, cells were incubated in the presence of AMD3100, PepE or PepK in the presence of CXCL12 plus Forskolin. CXCL12 100 ng/mL: maximal Gi protein activity; Forskolin 1 μM: maximal adenylate cyclase activity.

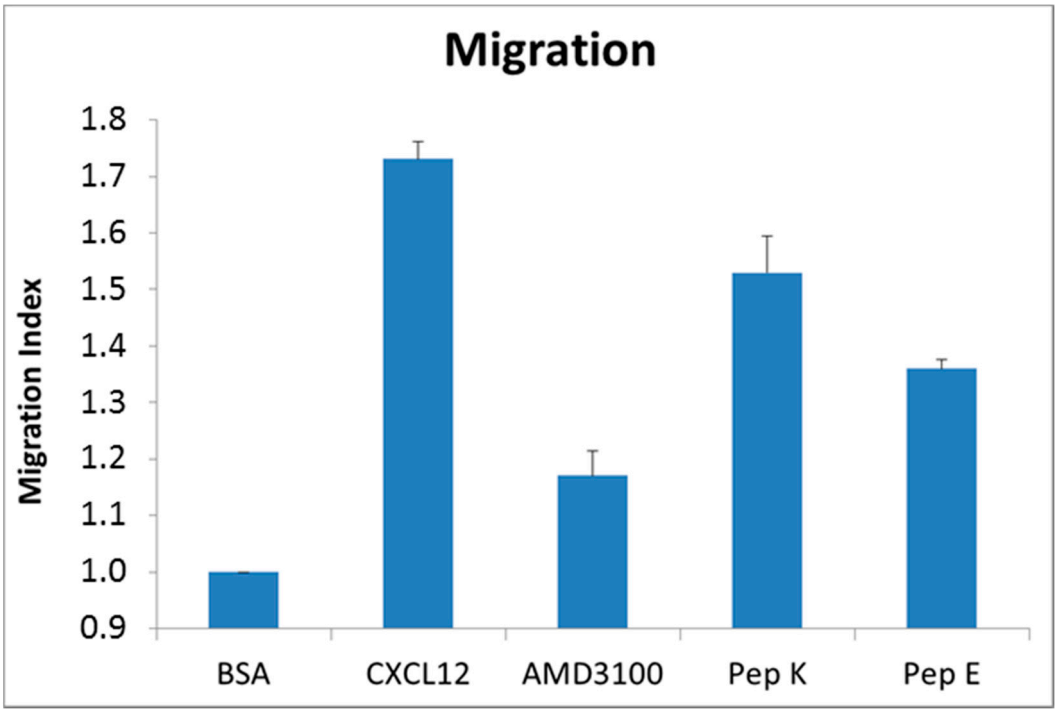

Figure S5. Migration assays. We report the migration index relative to migration in presence of BSA alone, and of CXCL12, AMD3100, PepK and PepE.