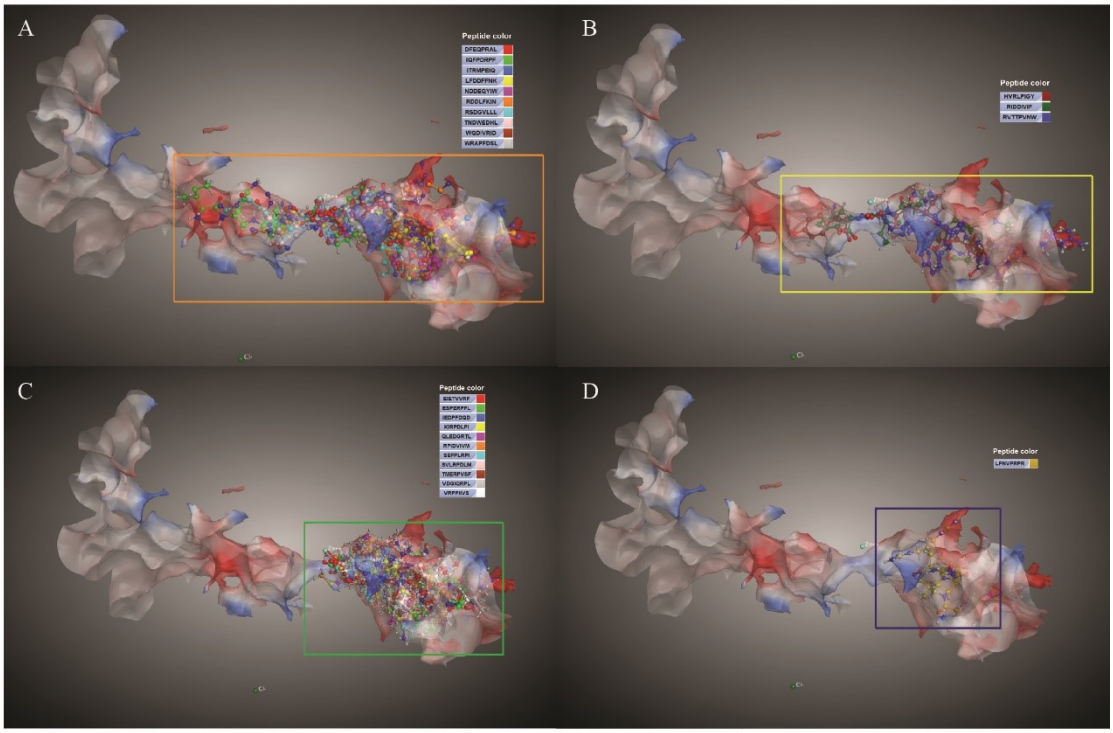

Fig. S1 2D binding plots of 25 octapeptides and the ACE receptor

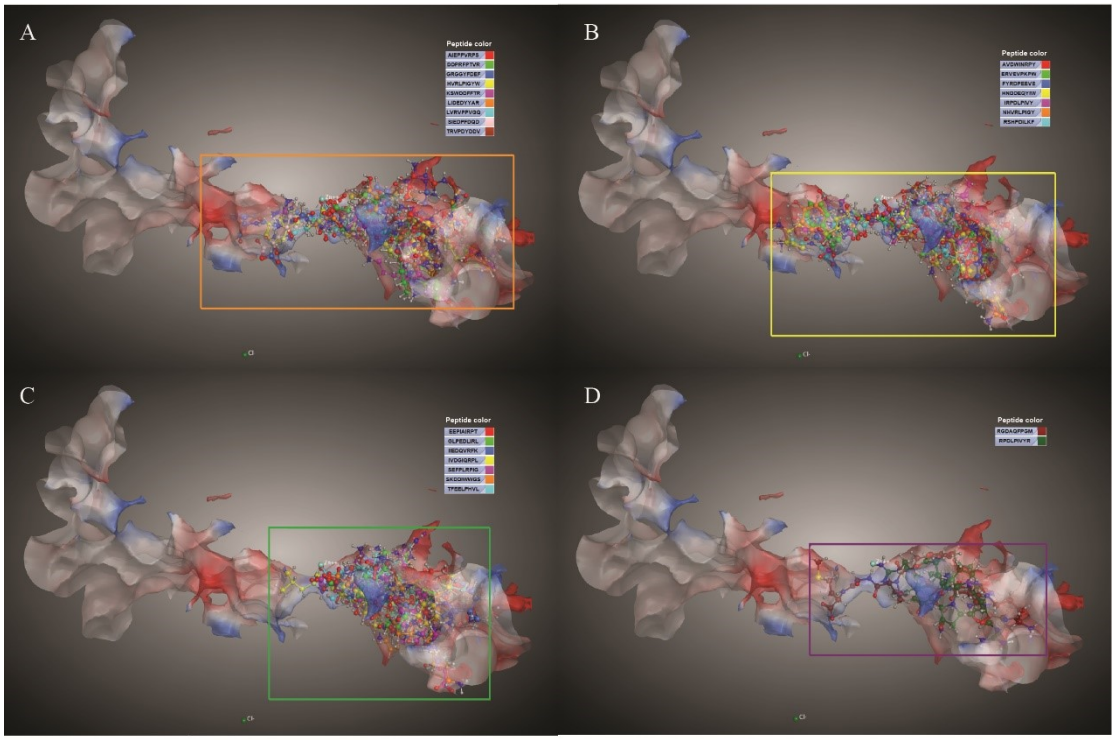

Fig. S2 2D binding plots of 25 nonapeptides and the ACE receptor

Table S1. Fifty oligopeptides information

Peptide sequence	Peptide molecular weight	Peptide chain length	Peptide secondary mass spectral abundance
DFEQPRAL	974.48	8	11500000
EIETVVRF	991.53	8	471000
ESPERPFL	973.49	8	9180000
HVRLPIGY	953.54	8	15100000
IEDPFDQD	977.40	8	991000
IQFPDRPF	1018.52	8	1130000
ITRMPEIQ	986.52	8	1620000
KIRPDLPI	950.59	8	2510000
LFDDFFNK	1044.49	8	840000
LPNVPRPR	947.57	8	95800
NDDEQYIW	1081.44	8	87200
QLEDGRTL	930.48	8	58500
RDDLFKIN	1019.54	8	13700000
RIDDIVIF	989.55	8	1880000
RPIDVIVM	941.54	8	2480000
RSDGVLLL	871.51	8	701000
RVTTPVNW	971.52	8	15500000
SEFPLRPI	957.53	8	80100000
SVLRPDLM	929.50	8	1720000
TMERPVSF	965.46	8	2270000
TNDWEDHL	1028.42	8	5450000
VDGIQRPL	896.51	8	188000
VRPPIIVS	879.55	8	3930000
WQDIVRID	1043.54	8	10500000
WRAPFDSL	990.49	8	1230000
AIEPPVRPS	964.53	9	1200000
AVDWINRPY	1132.57	9	2240000
DDPRFPTVR	1101.56	9	336000
EEPIAIRPT	1024.56	9	1070000
ERVEVPKPW	1138.61	9	695000
FYRDPEEVE	1182.52	9	234000
GLPEDLIRL	1024.59	9	105000
GRGGYFDEF	1046.45	9	6620000
HNDDEQYIW	1218.49	9	3200000
HVRLPIGYW	1139.62	9	311000
IIEDQVRFK	1146.64	9	481000
IRPDLPIVY	1084.63	9	2890000
IVDGIQRPL	1009.59	9	3590000
KSWDDFFTR	1200.56	9	22100000

LIDEDYYAR	1156.54	9	1140000
LVRVPPVGQ	963.59	9	5150000
NHVRLPIGY	1067.59	9	1420000
RGDAQFPGM	977.44	9	3920000
RPDLPIVYR	1127.65	9	272000
RSHPDILKF	1111.61	9	1540000
SEFPLRPIG	1014.55	9	23300000
SIEDPFDQD	1064.43	9	82700
SKDDIWWGS	1092.49	9	5130000
TFEELPHVL	1083.56	9	234000
TRVPDYDDV	1078.49	9	3140000

Table S2. The binding residues of two oligopeptides to the ACE receptor

	Binding amino acid residues in oligopeptide	Binding amino acid residues in the ACE receptor	Interaction mode	Distance between residues (Å)	Binding energy (kcal/mol)	Docking score
ESPERPFL	E1	ALA356	H-donor	2.99	-0.9	-13.39
	R5	GLU403	H-donor	2.83	-2.8	
	R5	GLU403	H-donor	3.23	-4	
	R5	GLU403	H-donor	3.04	-1.1	
	F7	GLU123	H-donor	3	-4.7	
	S2	ARG522	H-acceptor	3.22	-2.4	
	E4	ARG124	H-acceptor	2.98	-2.7	
	E4	ARG124	H-acceptor	3.23	-0.6	
	E1	ZN^{2+}	Metal	1.94	-6	
	E1	ZN^{2+}	Ionic	1.94	-17.5	
	E4	ARG124	Ionic	2.98	-4.6	
	E4	ARG124	Ionic	3.23	-3.1	
	R5	GLU403	Ionic	2.83	-5.7	
	R5	GLU403	Ionic	3.23	-3.1	
	R5	GLU403	Ionic	3.04	-4.2	
	E1	HIS387	cation-pi	4.18	-1.1	
KSWDDFFTR	K1	GLU143	H-donor	2.83	-11	-15.54
	S2	SER516	H-donor	3.49	-0.6	
	R9	GLU384	H-donor	3.43	-1.1	
	R9	GLU384	H-donor	3.3	-3.3	
	W3	ARG124	H-acceptor	2.94	-1.3	

D5	TRP59	H-acceptor	3.12	-0.5
D5	TYR62	H-acceptor	3.4	-0.5
R9	ZN^{2+}	Metal	1.9	-4.1
K1	GLU143	Ionic	2.83	-5.8
W3	ARG124	Ionic	3.57	-1.6
W3	ARG124	Ionic	3.16	-3.5
W3	ARG124	Ionic	3.46	-2.1
W3	ARG124	Ionic	3.22	-3.2
W3	ARG124	Ionic	2.89	-5.3
R9	GLU384	Ionic	3.3	-2.7
R9	ZN^{2+}	Ionic	1.9	-18.1
R9	HIS353	H-pi	4.24	-0.5
F6	ASN66	pi-H	3.2	-0.6
W3	ARG124	pi-cation	4.27	-1.9

Table S3. Binding modes of 50 oligopeptides and the ACE receptor

Binding modes	Oligopeptide	Peptide-binding amino acid residues in the receptor S1, S2, S1' active pockets	Binding energy with Zn^{2+}	Binding amino acid residues in peptides	3D plot	Bind properties
I	DFEQPRAL	ALA354	-18.1	D1	Figure S1 A	
I	IQFPDRPF	GLU384, GLN281, HIS353	-18.3	D5, Q2	Figure S1 A	
I	ITRMPEIQ	HIS353	-17.9	Q8	Figure S1 A	
I	LFDDFFNK	GLU384	-16.6	K8	Figure S1 A	Oligopeptides bound to the amino acid residues of S1, S2, S1'
I	NDDEQYIW	GLU162, GLU384, HIS353	-16.9	N1, D2, D3	Figure S1 A	
I	RDDLFKIN	GLU384, HIS353, TYR523	-11.4	R1, D2	Figure S1 A	Strong binding to Zn^{2+} (binding energy < -10 kcal/mol)
I	RSDGVLLL	ALA354	-18.9	D3	Figure S1 A	
I	TNDWEDHL	ALA354, GLN281	-18.2	D3, N2	Figure S1 A	
I	WQDIVRID	HIS353	-14.9	D8	Figure S1 A	
I	WRAPFDSL	HIS353, HIS513	-13.3	S7, D6, L8	Figure S1 A	
II	HVRLPIGY	HIS353, HIS513	-2.3	Y8, G7	Figure S1 B	Oligopeptides bound to the amino acid residues of S1, S2, S1'
II	RIDDIVIF	HIS353, HIS513	-1.1	F8, I7	Figure S1 B	
II	RVTTPVNW	GLU384	-3.8	N7	Figure S1 B	Moderately bound to Zn^{2+} (binding energy (E), -1 kcal/mol < E < -5 kcal/mol)
III	EIETVVRF	-	-15.6	F8	Figure S1 C	
III	ESPERPFL	-	-17.5	E1	Figure S1 C	
III	IEDPFDQD	-	-17.1	D8	Figure S1 C	Oligopeptides not bound to the amino acid residues of S1, S2, S1'
III	KIRPDLPI	-	-15.1	D5	Figure S1 C	
III	QLEDGRTL	-	-15.7	L8	Figure S1 C	Strongly bound to Zn^{2+} (binding energy < -10 kcal/mol)
III	RPIDVIVM	-	-14.9	M8	Figure S1 C	
III	SEFPLRPI	-	-18.0	E2	Figure S1 C	

III	SVLRPDLM	-	-16.6	D6	Figure S1 C	
III	TMERPVSF	-	-16.0	F8	Figure S1 C	
III	VDGIQRPL	-	-17.0	L8	Figure S1 C	
III	VRPPIIVS	-	-16.6	S8	Figure S1 C	
V	LPNVPRPR	-	-	-	Figure S1 D	Oligopeptides not bound to the amino acid residues of S1, S2, S1' Not bound to Zn^{2+}
I	AIEPPVRPS	ALA354	-15.7	S9	Figure S2 A	Oligopeptides bound to the amino acid residues of S1, S2, S1' Strong binding to Zn^{2+} (binding energy < -10 kcal/mol)
I	DDPRFPTVR	ALA354, GLU384	-15.6	R9	Figure S2 A	
I	GRGGYFDEF	ALA354, HIS513, LYS511	-12.2	F6, D7, E8	Figure S2 A	
I	HVRLPIGYW	GLU384, HIS353	-15.8	Y8, W9	Figure S2 A	
I	KSWDDFFTR	GLU384, HIS353	-18.1	R9	Figure S2 A	
I	LIDEDYYAR	GLU384	-18.8	R9	Figure S2 A	
I	LVRVPPVGQ	ALA354, TYR523	-18.3	Q9	Figure S2 A	
I	SIEDPFDQD	GLN281, LYS511	-16.6	D7, D9	Figure S2 A	
I	TRVPDYDDV	HIS353	-16.7	D8, V9	Figure S2 A	
II	AVDWINRPY	ALA354, HIS353	-1.6	A1, V2	Figure S2 B	Oligopeptides bound to the amino acid residues of S1, S2, S1' Moderately bound to Zn2+ (binding energy (E), -1 kcal/mol < E < -5 kcal/mol)
II	ERVEVPKPW	HIS513, GLN281, LYS511	-2.9	K7, P8, W9	Figure S2 B	
II	FYRDPEEVE	ALA354, GLN281, HIS353	-4.7	E7, V8, E9	Figure S2 B	
II	HNDDEQYIW	GLU162	-2.4	N2, D4	Figure S2 B	
II	IRPDLPIVY	GLN281, LYS511	-2.0	I7, Y9	Figure S2 B	
II	NHVRLPIGY	ALA354, HIS513, GLN281, LYS511	-2.8	I7, G8, Y9	Figure S2 B	
II	RSHPDILKF	GLU162, HIS513	-3.6	R1, S2, P4	Figure S2 B	
III	EEPIAIRPT	-	-17.2	E1	Figure S2 C	Oligopeptides not bound to the amino acid residues of S1, S2, S1'
III	GLPEDLIRL	-	-18.1	L9	Figure S2 C	

III	IIEDQVRFK	-	-18.0	K9	Figure S2 C	Strongly bound to Zn2+ (binding energy < -10 kcal/mol)
III	IVDGIQRPL	-	-14.3	L9	Figure S2 C	
III	SEFPLRPIG	-	-16.6	G9	Figure S2 C	
III	SKDDIWWGS	-	-17.6	S9	Figure S2 C	
III	TFEELPHVL	-	-14.8	L9	Figure S2 C	
IV	RGDAQFPGM	GLU384, GLN281, LYS511	-	-	Figure S2 D	Oligopeptides bound to the amino acid residues of S1, S2, S1' Not bound to Zn2+
IV	RPDLPIVYR	GLU384	-	-	Figure S2 D	

Note: - meant no binding information.