

Table S1 Selecting of the target crystal structures

Targets	Crystals (PPI)	Resolution	Unique Ligand	Contains site	Positions	Pocket integrity
AKTI	1UNQ	0.98 Å	4IP	-	1-123	
RAC-alpha	3O96	2.70 Å	IQO		2-443	
serine/threonine- protein kinase	4EJN	2.19 Å	0R4, SBT, EDO		2-446	
	4GV1	1.49 Å	0XZ, GOL		144-480	
MAPK8	2XRW	1.33 Å	ANP, GOL		2-364	
Mitogen-activated protein kinase 8	4YR8	2.40 Å	-		1-363	
MAPK10	3TTJ	2.10 Å	JBI		1-464	
Mitogen-activated protein kinase 10	4W4Y	2.30 Å	3HQ		39-402	
JUN Transcription factor AP-1	1JUN	-	-	-	276-314	
	1JNM	2.20 Å	-		254-315	
	1S9K	3.10 Å	-		257-308	
	1FOS	3.05 Å	-		254-315	

Note: “-” means there had no ligands, no resolution, no contains site, no pocket integrity could be found in the crystals.

Table S2 Molecular docking for GPPGPA and core targets, including mass, pI, hydrophilicity, binding targets and HPEPDOCK Score

Peptides	Molecular weight	pI	Hydrophilicity	Binding targets	HPEPDOCK Score
GPPGPA	494.55	5.52	-0.633	3O96-AKT1	-126.649
				2XRW-MAPK8	-115.549
				3TTJ-MAPK10	-122.139
				1JNM-JUN	-161.570

Table S3 Negative docking

NO.	Peptide	HPEPDOCK score			
		AKT1	MAPK8	MAPK10	JUN
1	GGAPPP	-131.948	-111.126	-109.827	-174.802
2	GGPPAP	-124.76	-111.071	-111.955	-176.202
3	GGPPPA	-125.898	-113.680	-118.552	-161.585
4	GGPAPP	-133.647	-111.587	-112.066	-177.377
5	GPGPAP	-130.312	-110.633	-114.083	-176.513
6	GPGPPA	-131.711	-111.516	-107.781	-170.345
7	GPGAPP	-133.762	-113.435	-111.275	173.673
8	GPAGPP	-133.841	-113.253	-118.052	-165.873
9	GPAPGP	-135.21	-112.426	-112.811	-164.498
10	GPAPPG	-124.038	-109.299	-112.165	-171.812
11	GPPGPA	-126.649	-115.549	-122.139	-161.57
12	GPPGAP	-131.642	-108.096	-119.388	-166.581
13	GPPPGA	-120.995	-115.116	-113.916	-159.509
14	GPPPAG	-129.7	-112.844	-108.185	-157.755
15	GPPAGP	-124.424	-111.784	-109.036	-163.253
16	GPPAPG	-132.355	-121.325	-117.92	-169.066
17	GAGPPP	-135.538	-108.024	-107.075	-171.59
18	GAPGPP	-123.587	-110.993	-108.834	-167.873
19	GAPPPG	-121.729	-125.618	-105.935	-159.3
20	GAPPGP	-125.704	-109.769	-108.821	-161.896
21	PGGPPA	-148.075	-123.873	-125.803	-184.802
22	PGGPAP	-144.065	-124.276	-125.426	-194.517
23	PGGAPP	-142.971	-118.888	-125.302	-183.511
24	PGPGPA	-149.191	-125.941	-131.596	-185.491
25	PGPGAP	-145.981	-125.266	-137.015	-189.67
26	PGPPGA	-140.681	-121.097	-127.254	-189.846
27	PGPPAG	-147.79	-124.704	-115.477	-193.462
28	PGPAGP	-151.416	-128.513	-127.021	-188.69
29	PGPAPG	-138.498	-118.193	-129.894	-191.904
30	PGAGPP	-133.327	-125.503	-124.289	-200.87
31	PGAPGP	-151.092	-124.877	-126.667	-198.09
32	PGAPPG	-139.475	-123.646	-122.364	-191.561
33	PPGGAP	-147.316	-133.275	-134.98	-186.397

34	PPGGPA	-150.732	-128.048	-130.738	-206.514
35	PPGPAG	-152.026	-129.187	-128.134	-176.203
36	PPGPGA	-164.452	-129.477	-131.539	-184.98
37	PPGAPG	-144.838	-136.154	-140.635	-193.796
38	PPGAGP	-148.525	-139.755	-130.989	-187.961
39	PPPGGGA	-149.623	-125.464	-130.898	-181.873
40	PPPAGAG	-145.158	-119.443	-137.729	-183.113
41	PPPAGG	-148.422	-123.859	-121.261	-191.363
42	PPAGGP	-148.724	-123.938	-119.934	-183.365
43	PPAGPG	-158.573	-133.769	-130.269	-183.203
44	PPAPGG	-154.771	-127.266	-123.858	-182.445
45	PAPGGP	-169.864	-125.925	-138.56	-190.728
46	PAPGPG	-152.593	-128.680	-129.66	-189.684
47	PAPPGG	-144.804	-131.712	-123.047	-191.473
48	PAGGPP	-145.776	-120.606	-129.991	-190.546
49	PAGPPG	-158.431	-126.073	-135.34	-187.999
50	PAGPGP	-160.481	-127.451	-121.789	-187.013
51	APGGPP	-131.188	-108.886	-118.256	-172.674
52	APGPGP	-137.627	-109.847	-112.988	-170.096
53	APGPPG	-129.07	-113.571	-113.457	-174.315
54	APPGPG	-127.334	-118.132	-121.826	-176.491
55	APPGGP	-134.97	-115.463	-109.217	-165.888
56	APPPGG	-128.716	-123.250	-114.978	-157.288
57	AGGPPP	-126.95	-104.120	-112.458	-177.039
58	AGPGPP	-134.816	-116.961	-111.709	-166.405
59	AGPPGP	-129.164	-111.317	-123.474	-177.773
60	AGPPPG	-129.419	-112.071	-114.441	-175.771

AKT1: 52/60

MAPK8: 36/60

MAPK10: 28/60

JUN: 55/60