

Pharmaceuticals

SUPPLEMENTARY MATERIALS

In Silico Studies on GCP-Lys-OMe as a Potential 14-3-3 σ Homodimer Stabilizer

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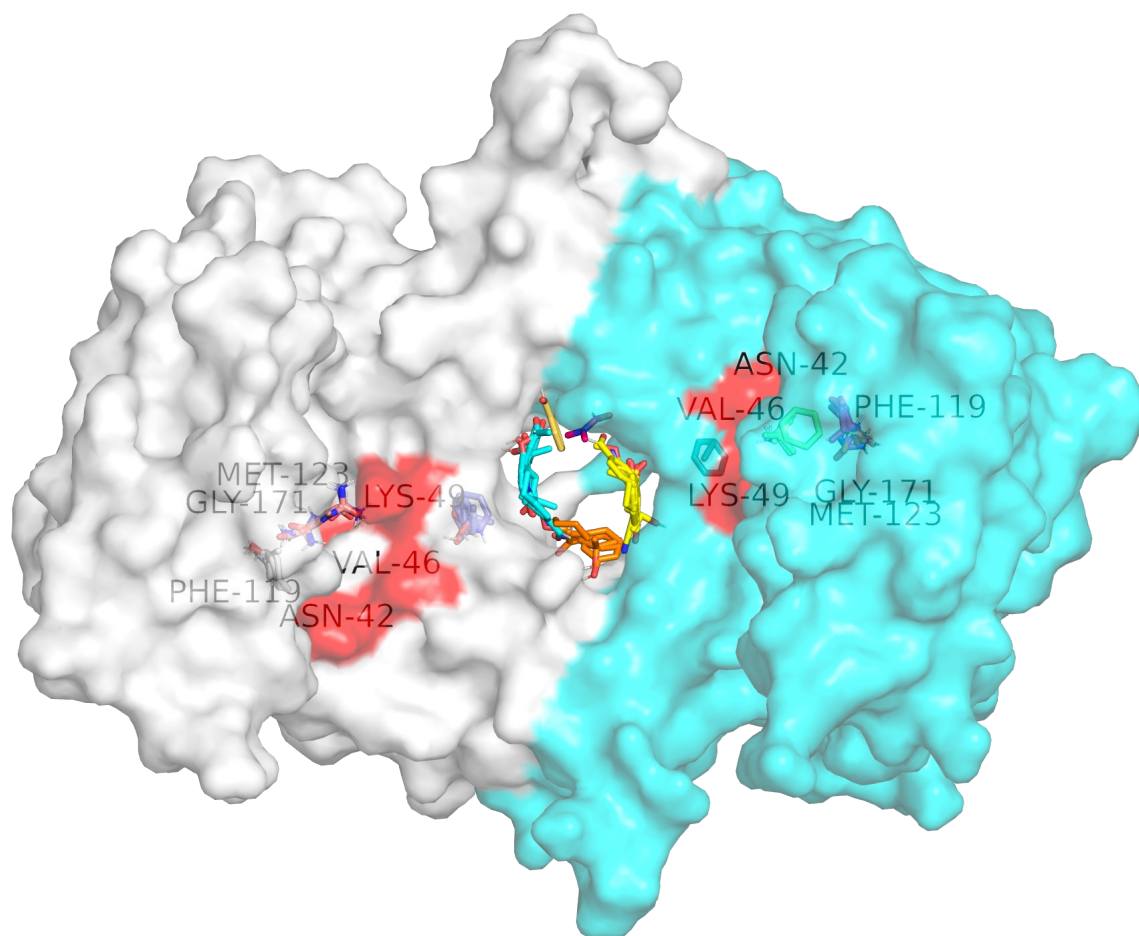


Figure S1. 14-3-3 σ binding hotspots by FTMap. Residues lining the amphipathic ligand binding pockets of 14-3-3 σ homodimer (white/cyan surface) are labeled, with key interacting residues highlighted in red. The probes (shown in sticks) are mainly bound at the center cavity of the homodimer interface and the amphipathic pockets (monomer A and monomer B) of 14-3-3 σ .

Table S1. Hydrogen bond pairs between monomers of 14-3-3 σ in apo and GCP-Lys-OMe-bound systems at 100 ns simulation. Only the residues at H1-H4 (the dimer interface) are shown. Similar pairs (i.e. involving the same residues) between the two systems are bolded.

System	Pair ID	Donor - Acceptor	Atom number
Apo (14-3-3 σ alone)	1	84TYR(HH) – 21ASP(OD1)	3177 - 218
	2	77LYS(HZ1) – 8GLN(OE1)	3100 - 77
	3	9LYS(HZ1) – 83GLU(OE2)	2425 - 825
	4	9LYS(HZ1) – 83GLU(OE1)	2425 - 824
	5	8GLN(E21) – 77LYS(O)	2413 - 770
	6	84TYR(HH) – 21ASP(OD2)	843 - 2553
	7	18ARG(H21) – 91GLU(OE2)	181 - 3254
	8	18ARG(H11) – 55GLN(OE1)	178 - 2870
Bound (14-3-3 σ /GCP-Lys-OMe complex)	1	84TYR(HH) – 21ASP(OD1)	3177 - 218
	2	69SER(H) – 8GLN(OE1)	3021 - 77
	3	68LYS(HZ1) – 15GLN(OE1)	3015 - 146
	4	18ARG(H21) – 91GLU(OE2)	2515 - 920
	5	18ARG(H21) – 91GLU(OE1)	2515 - 919
	6	18ARG(H11) – 91GLU(OE1)	2512 - 919
	7	18ARG(H11) – 55GLN(NE2)	2512 - 537
	8	18ARG(HE) – 84TYR(OH)	2509 - 842
	9	84TYR(HH) – 21ASP(OD1)	843 - 2552
	10	11LYS(HZ1) – 70ASN(OD1)	110 - 3033
	11	9LYS(HZ1) – 83GLU(OE1)	91 - 3158
	12	8GLN(E21) – 80GLU(OE1)	79 - 3123
	13	8GLN(E21) – 68LYS(O)	79 - 3019

Table S2. Hydrogen bond occupancy between monomers of 14-3-3 σ in apo system throughout the whole 100 ns simulation. Only the residues at H1-H4 (the dimer interface) are shown.

Pair ID	Donor - Acceptor	Atom number	Hydrogen bond occupancy (%)
1	84TYR(HH) – 21ASP(OD2)	843 - 2553	45.8
2	84TYR(HH) – 21ASP(OD1)	843 - 2552	39.8
3	84TYR(HH) – 21ASP(OD2)	3177 - 219	37.9
4	84TYR(HH) – 21ASP(OD1)	3177 - 218	37.9
5	9LYS(HZ1) – 83GLU(OE2)	91 - 3159	29.3
6	9LYS(HZ1) – 83GLU(OE1)	91 - 3158	28.1
7	80GLU(H) – 8GLN(OE1)	784 - 2411	23.5
8	18ARG(H11) – 84TYR(OH)	2512 - 842	20.1
9	18ARG(HE) – 84TYR(OH)	175 - 3176	19.9
10	9LYS(HZ1) – 83GLU(OE1)	2425 - 824	19.1
11	9LYS(HZ1) – 83GLU(OE2)	2425 - 825	17.6
12	18ARG(HE) – 84TYR(OH)	2509 - 842	17.5
13	18ARG(H11) – 55GLN(OE1)	2512 - 536	17.1
14	18ARG(H21) – 55GLN(OE1)	2515 - 536	15.6
15	18ARG(H11) – 55GLN(OE1)	178 - 2870	13.7
16	5SER(HG) – 80GLU(OE2)	2384 - 790	11.5
17	18ARG(H21) – 55GLN(OE1)	181 - 2870	10.5
18	5SER(HG) – 80GLU(OE1)	2384 - 789	10.1
19	8GLN(E21) – 74SER(O)	79 - 3071	10.0

Table S3. Hydrogen bond occupancy between monomers of 14-3-3 σ in GCP-Lys-OMe-bound systems throughout the whole 100 ns simulation. Only the residues at H1-H4 (the dimer interface) are shown.

Pair ID	Donor - Acceptor	Atom number	Hydrogen bond occupancy (%)
1	84TYR(HH) – 21ASP(OD2)	3177 - 219	43.0
2	15GLN(E21) – 69SER(OG)	148 - 3024	36.9
3	84TYR(HH) – 21ASP(OD1)	843 - 2552	36.8
4	84TYR(HH) – 21ASP(OD2)	843 - 2553	35.9
5	84TYR(HH) – 21ASP(OD1)	3177 - 218	35.8
6	18ARG(H11) – 55GLN(OE1)	178 - 2870	28.8
7	9LYS(HZ1) – 83GLU(OE1)	2425 - 824	28.5
8	9LYS(HZ1) – 83GLU(OE2)	2425 - 825	27.5
9	9LYS(HZ1) – 83GLU(OE2)	91 - 3159	27.5
10	68LYS(HZ1) – 15GLN(OE1)	3015 - 146	26.1
11	9LYS(HZ1) – 83GLU(OE1)	91 - 3158	25.4
12	18ARG(H11) – 55GLN(OE1)	2512 - 536	24.2
13	18ARG(HE) – 84TYR(OH)	175 - 3176	19.8
14	18ARG(HE) – 84TYR(OH)	2509 - 842	15.8
15	70ASN(H) – 15GLN(OE1)	3029 - 146	14.1
16	69SER(H) – 8GLN(OE1)	3021 - 77	13.5
17	18ARG(H21) – 55GLN(OE1)	181 - 2870	12.4
18	8GLN(E21) – 68LYS(O)	79 - 3019	11.4
19	8GLN(E21) – 75GLU(O)	79 - 3081	11.1
20	18ARG(H11) – 84TYR(OH)	178 - 3176	11.1
21	11LYS(HZ1) – 71GLU(OE1)	110 - 3045	10.8
22	18ARG(H21) – 91GLU(OE1)	2515 - 919	10.3
23	11LYS(HZ1) – 71GLU(OE2)	110 - 3046	10.1

Table S4. Hydrogen bond occupancy between monomers of 14-3-3 σ and GCP-Lys-OMe in GCP-Lys-OMe-bound systems throughout the whole 100 ns simulation. Only the residues at H1-H4 (the dimer interface) are shown.

Pair ID	Donor - Acceptor	Atom number	Hydrogen bond occupancy (%)
1	20GLU(H) – 234UNK(O20)	2538 - 4695	61.8