Computational Insights into the Binding of IN17 Inhibitors to MELK

Matthew Harger[1], Ju-Hyeon Lee[2], Brandon Walker[1], Juliana M Taliaferro[2] Ramakrishna Edupuganti[2], Kevin N. Dalby[2], Pengyu Ren[1]

1 Department of Biomedical Engineering, The University of Texas at Austin, Austin, Texas, 78712, United States
2 Division of Chemical Biology and Medicinal Chemistry, University of Texas at Austin, Austin, TX 78712, United States

Supplementary Information

Table S1a:

Vdw-lambda/ele-lambda, and group restraints sed for binding phase simulations

Vdw-lambda	Ele-lambnda	Group restraint
1.0	1.0	0.0
1.0	0.95	1.0
1.0	0.9	2.0
1.0	0.8	4.0
1.0	0.7	6.0
1.0	0.6	8.0
1.0	0.5	10.0
1.0	0.4	12.0
1.0	0.3	14.0
1.0	0.2	15.0
1.0	0.1	15.0
1.0	0.0	15.0
0.95	0.0	15.0
0.9	0.0	15.0
0.85	0.0	15.0

0.8	0.0	15.0
0.75	0.0	15.0
0.70	0.0	15.0
0.65	0.0	15.0
0.63	0.0	15.0
0.61	0.0	15.0
0.59	0.0	15.0
0.57	0.0	15.0
0.55	0.0	15.0
0.5	0.0	15.0
0.4	0.0	15.0
0.0	0.0	15.0

Table S1b:

Vdw-lambda/ele-lambda, group restraint, and torsion restrains used for solvation phase simulations

Vdw-lambda	Ele-lambnda	Torsion restraint
1.0	1.0	0.0
1.0	0.9	0.0
1.0	0.8	0.0
1.0	0.7	0.0
1.0	0.6	0.0
1.0	0.5	0.0
1.0	0.4	0.0
1.0	0.3	0.0
1.0	0.2	0.0
1.0	0.1	0.0
1.0	0.0	0.0
0.9	0.0	0.01
0.8	0.0	0.02
0.75	0.0	0.03
0.7	0.0	0.04
0.65	0.0	0.05
0.62	0.0	0.06
0.6	0.0	0.07
0.55	0.0	0.08
0.5	0.0	0.09
0.4	0.0	0.1
0.0	0.0	0.1

	binding enthalpy	binding enthalpy error	binding entropy (TΔS)	solvation enthalpy	solvation enthalpy error	solvation entropy TΔS	ΔH	TΔS

16	-149.8	32.8	-76.4	**-77.4**	27.1	-22.8	-72.3	-53.6
22	-150.8	43.6	-73.7	-34.8	31.3	27.6	-116.0	-101.3
25	-127.7	37.1	-44.6	-100.5	28.8	-34.5	-27.2	-10.1
18a	-131.7	36.9	-61.3	-131.1	28.9	-78.2	-0.6	16.9
18b	-121.4	36.8	-41.3	-66.7	29.5	-4.9	-54.7	-36.3
18d	28.5	80.8	-110.3	-123.8	29.1	60.0	152.2	-170.4
18e	-120.8	80.6	-40.1	-172.2	29	-111.5	51.5	71.4
18g	-106.1	35.6	-24.7	-47.0	28.4	17.0	-59.1	-41.6
18i	-85.9	36.6	-8.3	-128.5	30.6	-69.6	42.6	61.3
18p	-273.6	36.4	-203.8	-84.1	28.5	-32.9	-189.6	-170.9
IN17	-94.9	32.9	-23.3	-115.1	15.1	-63.1	20.2	39.8

Table S2: Calculated binding and solvation entropy and enthalpy

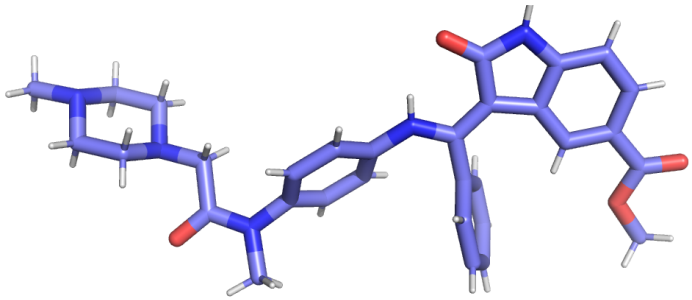

Figure S1: Solvent phase crystal structure of IN17