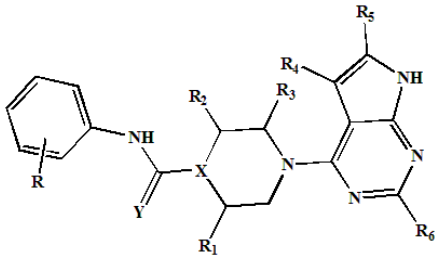
Electronic Supplementary Material (ESI) for Molecular BioSystems

Supporting Materials

Table S1. The structures of 41 inhibitors



No.	X	Y	R	R_1	R_2	R_3	R_4	R_5	R_6	pIC_{50}
1	CH	O	H	H	H	H	Me	H	H	6.1
5a*	CH	O	2-Me	H	H	H	Me	H	H	4.94
5b*	CH	O	3-Me	H	H	H	Me	H	H	6.19
5c*	CH	O	4-Me	H	H	H	Me	H	H	5.89
5d*	CH	O	3-OMe	H	H	H	Me	H	H	6.28
5e*	CH	O	4-OMe	H	H	H	Me	H	H	5.82
5f	CH	O	3-OPh	H	H	H	Me	H	H	7.19
5g*	CH	O	3-Br	H	H	H	Me	H	H	6.52
11a*	N	O	3-Me	H	H	H	Me	H	H	7.04
11b*	N	O	3-OMe	H	H	H	Me	H	H	6.85
11c*	N	O	3-Br	H	H	H	Me	H	H	7.42
12*	N	NCN	3-Br	H	H	H	Me	H	H	7.96
13*	N	O	3-Br	(S)-Me	H	H	Me	H	H	8.41
14*	N	NCN	3-Br	(S)-Me	H	H	Me	H	H	9.05
15*	N	O	3-Br	(S)-Me	H	H	Me	H	H	7.43
16*	N	NCN	3-Br	(S)-i-Pr	H	H	Me	H	H	8.38
17	N	NCN	3-Br	Me(trans)	H	Me	Me	H	H	8.41
18	N	O	3-Br	Me(cis)	Me	H	Me	H	H	6.88
19	N	O	3-Br	$-CH_2CH_2-$	$-CH_2CH_2-$	H	Me	H	H	7.80
20	N	NCN	3-Br	$-CH_2-$	H	$-CH_2-$	Me	H	H	7.12
21a	N	NCN	3-Br	(S)-Me	H	H	H	H	H	8.09
21b*	N	NCN	3-Br	(S)-Me	H	H	Cl	H	H	8.92
21c	N	NCN	3-Br	(S)-Me	H	H	H	Me	H	8.38
22a*	N	NSO_2Me	3-Br	(S)-Me	H	H	Me	H	H	8.17
22b	N	NCN	3-Cl	(S)-Me	H	H	Me	H	H	8.8
22c	N	O	3-Cl	(S)-Me	H	H	Me	H	H	8.64
22d	N	NCN	3-F	(S)-Me	H	H	Me	H	H	8.74
22e	N	NCN	3-Br,4-F	(S)-Me	H	H	Me	H	H	8.82
22f	N	O	3-Br,4-F	(S)-Me	H	H	Me	H	H	8.49
22g	N	NCN	$3-CF_3$	(S)-Me	H	H	Me	H	H	8.72
22h	N	NCN	3-CN	(S)-Me	H	H	Me	H	H	8.92

22i	N	NCN	3-t-Bu	(S)-Me	H	H	Me	H	H	8.96
22j	N	O	3-OCONMe$_2$	(S)-Me	H	H	Me	H	H	8.92
22k	N	NCN	3-CONH-i-Pr	(S)-Me	H	H	Me	H	H	8.46
22l	N	O	3-CONH-i-Pr	(S)-Me	H	H	Me	H	H	8.26
22m*	N	NCN	3-CONH(CH2)$_2$OH	(S)-Me	H	H	Me	H	H	9.10
22n	N	O	3-CONH(CH2)$_2$OH	(S)-Me	H	H	Me	H	H	8.52
22o	N	O	3-CONHCH(CH$_2$OH)$_2$	(S)-Me	H	H	Me	H	H	8.52
22p	N	NCN	3-CONH(CH$_2$)$_2$NMe$_2$	(S)-Me	H	H	Me	H	H	8.47
22q	N	NCN	SO$_2$NH-i-Pr	(S)-Me	H	H	Me	H	H	8.77
22r	N	NCN	SO$_2$NH(CH$_2$)$_2$OH	(S)-Me	H	H	Me	H	H	8.54

*Molecules selected for the MD simulations and free energy calculations

Table S2. The predicted binding free energies and the individual energy components for the studied molecules based on the solute dielectric constant of 1 (kcal/mol)

No.	ΔE_{vdw}	ΔE_{ele}	ΔG_{SA}	ΔG_{GB}	ΔG_{pred}	pIC_{50}
22m	-53.71±3.50	-52.02±5.13	-7.59±0.36	64.24±3.42	-49.09±3.31	9.10
14	-50.95±2.94	-26.53±6.28	-6.53±0.13	42.45±4.78	-41.56±2.92	9.05
21b	-52.61±3.63	-22.02±5.82	-6.42±0.21	37.81±4.17	-43.23±3.92	8.92
13	-48.68±3.14	-7.99±6.35	-6.27±0.12	25.54±5.48	-37.39±2.59	8.41
16	-56.03±3.57	-34.29±2.93	-6.79±0.08	49.42±3.42	-47.85±2.38	8.38
22a	-50.10±2.78	-24.04±7.17	-6.96±0.18	46.34±6.67	-34.76±2.89	8.17
12	-50.49±2.72	-31.37±5.01	-6.47±0.21	48.64±4.15	-39.68±2.74	7.96
15	-45.35±3.11	-17.94±5.24	-6.47±0.17	33.25±4.30	-36.51±3.11	7.43
11c	-52.50±3.76	-7.78±6.40	-6.07±0.13	27.03±5.89	-39.31±3.29	7.42
11a	-40.42±3.21	-6.56±4.71	-6.08±0.17	20.66±3.56	-32.41±2.81	7.04
11b	-47.08±2.96	-7.95±3.21	-6.44±0.28	25.52±2.69	-35.96±2.82	6.85
5g	-44.55±3.28	-27.62±10.43	-6.16±0.19	42.25±9.06	-36.08±3.99	6.52
5d	-46.88±4.42	4.12±11.50	-6.75±0.30	15.31±11.87	-34.20±3.58	6.28
5b	-47.94±3.49	-13.31±4.71	-5.90±0.17	31.73±4.12	-35.42±3.26	6.19
5c	-43.49±3.68	-13.17±5.72	-6.54±0.20	30.75±5.77	-32.45±3.47	5.89
5e	-46.76±2.83	-22.15±3.86	-6.41±0.12	40.31±2.76	-35.01±2.78	5.82
5a	-41.79±4.74	-14.52±6.39	-5.75±0.28	31.01 ±6.18	-31.06±4.68	4.94

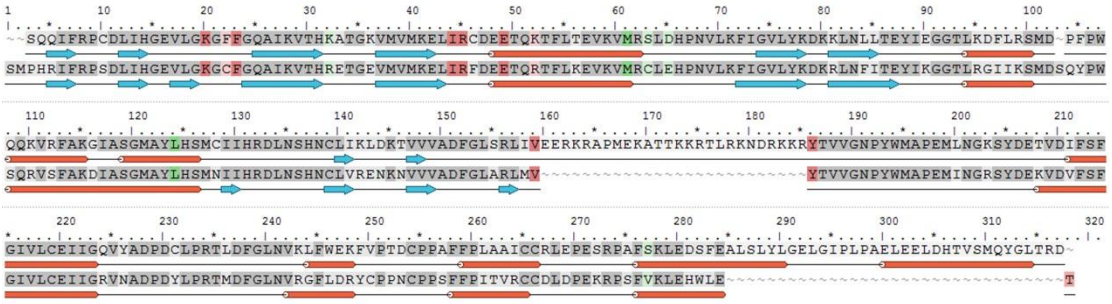


Figure S1. The sequence alignment between LIMK1 and LIMK2.

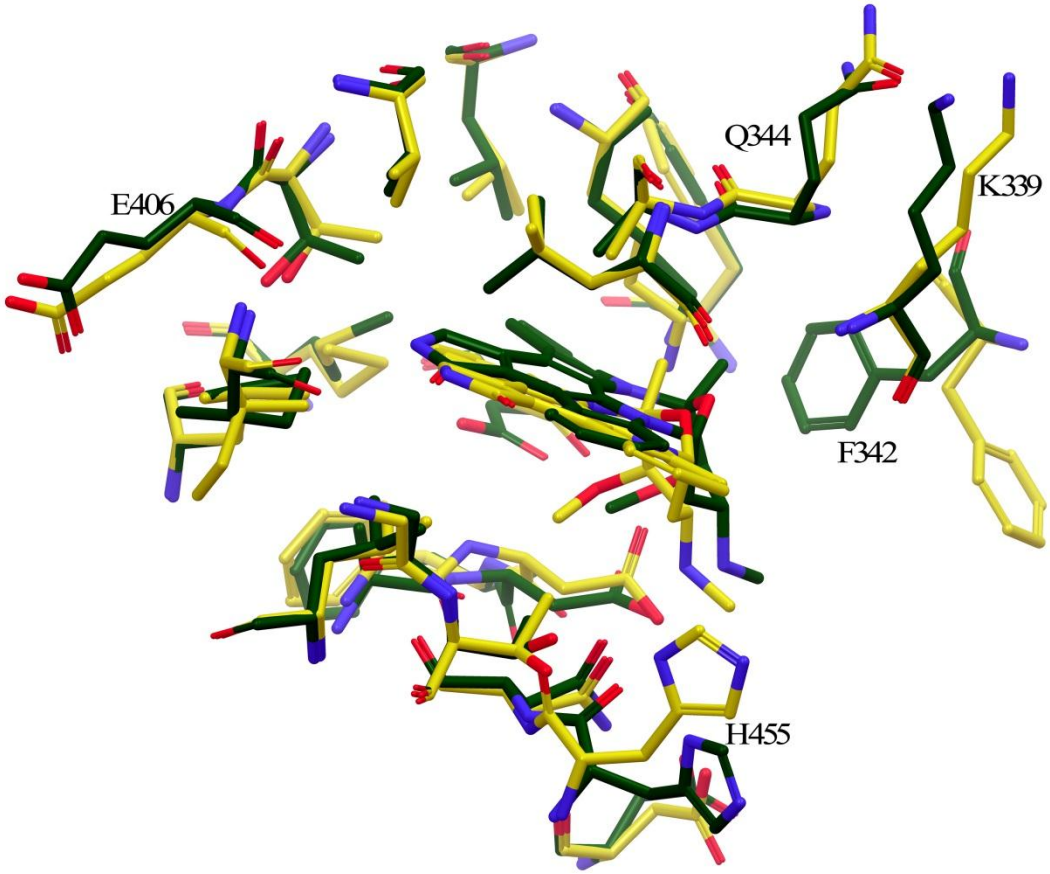


Figure S2. The docked pose of staurosporine predicted by *IFD* in the active site of LIMK2 overlapped with its original structure in the homology model (carbon atoms in the homology model are colored in dark green, and those in the docked structure in yellow).

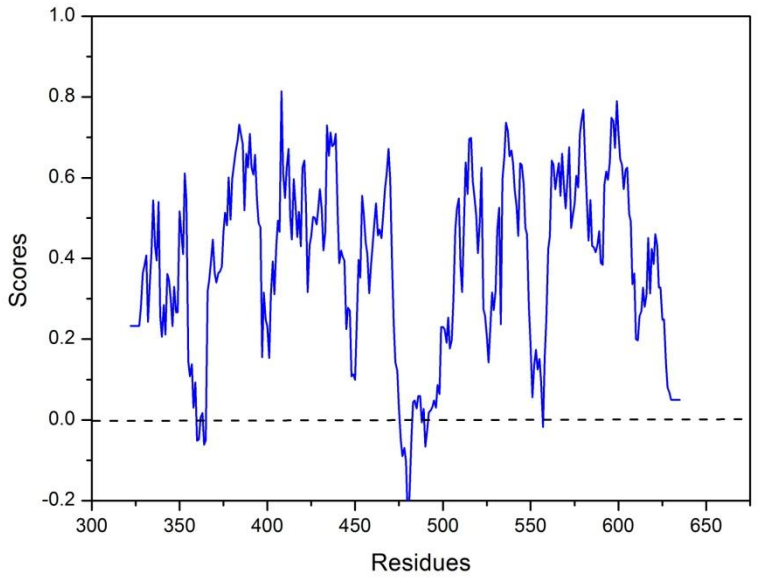


Figure S3. The Profile-3D scores for the LIMK2 structure generated by homology modeling

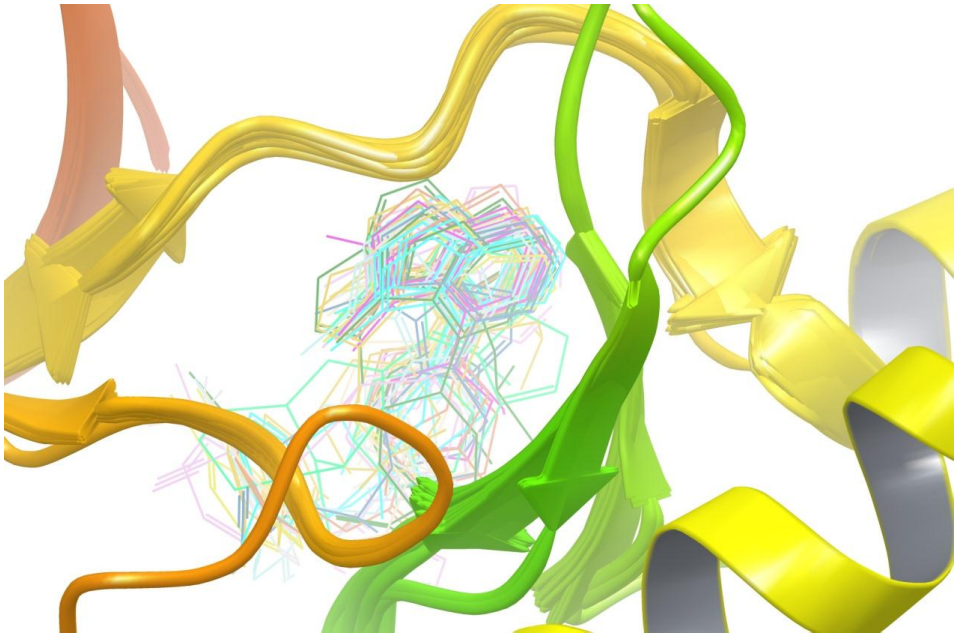


Figure S4. The alignments of 41 docked structures in the binding site of LIMK2.